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THE ISOLATION OF CANCER CELLS FROM THE BLOOD STREAM DURING UTERINE CURETTAGE

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CANCER CELLS are carried from the primary site to distant parts of the body via the blood stream at some stage in the natural history of many malignant tumors. The belief that this vascular dissemination of cancer cells occurs in 10 to 15 per cent of patients with endometrial carcinoma is based on the reported incidence of pulmonary metastases associated with this malignant tumor.

Uterine curettage is performed almost routinely in the diagnostic evaluation of patients suspected of having endometrial carcinoma. Some investigators have criticized curettage in such cases of suspected endometrial carcinoma on the grounds that it might result in the dissemination of cancer cells through vascular channels, lymphatic channels, or the open ends of the fallopian tubes. Others have pointed out that, although this might be theoretically possible, there is more danger in not performing a curettage and thereby missing a cancer. Endometrial carcinoma can be detected by vaginal cytologic examination in as many as 75 per cent of the cases, whereas endometrial aspiration yields 85 per cent detection. Irrespective of the results obtained by the cytologic method, however, it is a generally accepted principle that curettage is performed for confirmation.

This study is a continuation of laboratory work in which "showers" of cancer cells have been isolated from the blood stream during various forms of operative manipulation. The patients included in this report have been studied during diagnostic curettage of various malignant and benign lesions of the uterus in an effort to elucidate whether the vascular dissemination of cancer cells during curettage is a theoretic or factual possibility.

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METHODS

Collection of blood samples. Samples of peripheral blood are obtained from the antecubital veins. Samples of blood from veins draining the uterus are obtained from the inferior vena cava (Fig. 1). A 14 gauge thin walled needle is inserted into the femoral

TABLE I.—SUMMARY OF 10 PATIENTS STUDIED DURING UTERINE CURETTAGE

Case No.		*Blood sample*	*Results*
	MALIGNANT DISEASES		
1	Epidermoid carcinoma of cervix	Peripheral	Negative
2	Carcinoma in situ of cervix	Vena cava	Negative
3	Adenocarcinoma of cervix and uterus*	Vena cava	Positive
4	Adenocarcinoma of cervix and uterus*	Vena cava	Positive
5	Adenocarcinoma of uterus	Peripheral	Negative
6	Adenoacanthoma of uterus	Vena cava	Positive
7	Adenocarcinoma of ovary involving the uterus	Peripheral	Positive
	BENIGN DISEASES		
8	Hyperplastic endometrium	Peripheral	Negative
9	Leiomyoma of uterus	Peripheral	Negative
10	Hydatidiform mole	Peripheral	Negative

*These 2 patients had extension of the carcinoma outside the uterus with no evidence of hematogenous spread.

vein, and a measured segment of 18 gauge heparinized polyethylene tubing is threaded through the needle into the vena cava to the level of the umbilicus. Coagulation of blood in the polyethylene tubing is prevented by maintaining a drip of 250 cubic centimeters of 5 per cent glucose in saline to which 10 milligrams of the anticoagulant heparin has been added.

Isolation of cancer cells. The previously published (14) method for the isolation of cancer cells from whole blood is based on the principle that many cancer cells are lighter than leucocytes and therefore can be separated by albumin flotation. Although the method is not quantitative, careful identical processing of all blood samples permits comparison.

In 1 patient with carcinoma in situ of the cervix a simpler, more quantitative method previously described (10) was used in which streptolysin-0 was utilized to lyse erythrocytes and polymorphonuclear leucocytes, leaving cancer cells and lymphocytes. The slides were immediately immersed in ether and alcohol and stained according to the Papanicolaou technique. The slides are scanned by technicians and all cells thought to be malignant are checked by one of us who is a professional cytologist. The cancer cells isolated from the blood stream are compared to a direct smear of the tumor (Fig. 2).

RESULTS

The 10 patients with various malignant and benign diseases of the uterus were studied during curettage. Fifty-two blood samples were drawn from these 10 patients (8 slides per blood sample). Three of the patients had histologic diagnoses of benign lesions—hyperplastic endometrium, leiomyoma of the uterus, and hydatidiform mole. No abnormal cells were found in the blood from these 3 patients during curettage. Cancer cells were found in the blood stream during curettage in 4 of the 5 patients with a histologic and cytologic diagnosis of malignant disease involving the endometrium, as seen in Table I.

In the first 2 patients, 1 with epidermoid carcinoma of the cervix and the other with carcinoma in situ, no circulating cancer cells were detected during curettage. The second patient was studied by a newer method of isolation, and only cells interpreted as megakaryocytes were seen other than the usual formed blood elements. The third patient, with adenocarcinoma involving the corporeal endometrium and endocervix, had blood samples drawn via catheter from the inferior vena cava every 2 minutes during curettage, as seen in Figure 3. Cancer cells were first isolated from the fourth blood sample taken during dilatation of the cervix. More cancer cells were isolated during curettage of the endocervix and endometrium (Fig. 4) and none were found within 2 minutes after finishing curettage. Similar findings were present in the fourth patient with adenocarcinoma involving the corporeal endometrium and endocervix. No cancer cells were found in the blood samples from the antecubital vein during curettage in the fifth patient with adenocarcinoma of the uterus.

In the sixth patient, with adenoacanthoma of the uterus, blood samples were drawn from the inferior vena cava every 2 minutes during curettage, as seen in Figure 5. There were 5 negative blood samples prior to the 1 positive blood sample which was drawn slowly at the moment the clini-

cian stated that he was "scraping gritty tissue at 6:00 o'clock" (Fig. 6). Two minutes later no cancer cells were found and all subsequent samples were noted to be negative.

The seventh patient, with ovarian carcinoma involving the uterus was studied by serial peripheral blood samples from the antecubital vein. Eleven days preoperatively no cancer cells were found. At the time of pelvic examination under anesthesia, the clinician inadvertently ruptured a tumor mass, and a shower of cancer cells was seen after this pelvic examination. Again, during curettage, an increased number of cancer cells was isolated. At celiotomy, it was apparent that a cystadenocarcinoma of the ovary had been ruptured and that the tumor had invaded the uterine fundus. Fragments of tumor were present in the curettage material. More cancer cells were found during operation than at any time during the previous blood sampling, and relatively few cancer cells were found at the time the tumor was removed. No cancer cells were found 2 days postoperatively.

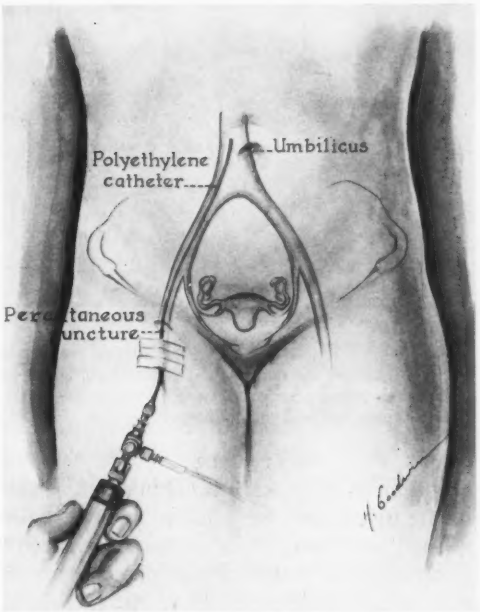


FIG. 1. Blood samples are collected from the inferior vena cava via a plastic catheter inserted through a needle cutdown of the femoral vein.

DISCUSSION

The demonstration of cancer cells in the blood stream during curettage adds information to several phases in the vascular dissemination of endometrial carcinoma. In general, the dissemination of cancer by vascular channels may be considered as occurring in a sequence of four phases, as shown diagrammatically in Figure 7: (1) entrance of cancer cells into vascular channels by invasion of the blood vessels or lymphatic tributaries of the veins, or by a mechanical intravasation, followed by (2) transportation of single or clumps of cancer cell emboli from the primary site to distant parts of the body via the circulating blood, where there is (3) lodgement of the cancer cells in arterioles and capillaries of the various tissues and organs where the (4) fate of many of the transported cancer cells is death; others manage survival and establish a metastasis.

A prerequisite to the formation of hematogenous metastases is the entrance of cancer cells of the primary tumor into vascular channels by any or all of three routes. Invasion via two of these routes—the blood vessels and the lymphatic tributaries of veins—is the result of invasive growth. The third route is based on a principle of increased extravascular pressure which results in the mechanical intravasation of cancer cells and, at times, nonneoplastic cells, placing them within disrupted vascular channels without the presence of vascular invasion. These means of entry can be summarized as follows (Fig. 7): (1) invasion of blood vessels; (2) invasion of lymphatic tributaries of veins; and (3) mechanical intravasation.

The invasion of blood vessels is the most obvious route of entry. Javert reported that 8 of 50 patients, or 16 per cent, with endometrial carcinoma had cancer emboli within the uterine blood vessels. He also

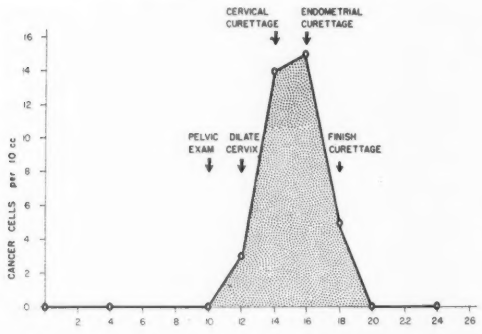


FIG. 3. Case 3. Cancer cells in the inferior vena cava during dilatation and curettage. The histologic diagnosis of this patient was adenocarcinoma involving the corporeal endometrium and the endocervix.

emphasized that thin walled blood vessels of the uterus may be invaded in superficial as well as in deep myometrial involvement. Trophoblastic tissue of the placenta, even that of a normal pregnancy, also has invasive properties and is capable of penetrating blood vessels and may be transported in the blood stream to the lungs.

The second route of entry is the result of neoplastic invasion of lymphatic tributaries of veins, the most prominent of which is the thoracic duct. In the series reported by Javert (6, 7) 14 of 50 patients, or 28 per cent, with endometrial carcinoma had metastases to the pelvic lymph nodes. He made the important observation that in 5 of these patients, or 10 per cent, paranodal vascular invasion was present.

The third route of entry, mechanical intravasation, places cancer cells and, at times, normal tissue cells within vascular channels without the presence of vascular invasion. It has generally been assumed that the entrance of cancer cells into vascular channels is the exclusive consequence of their invasive growth, even though a careful histologic examination of the primary tumor fails to demonstrate vascular or lymphatic invasion. However, the embolization of normal tissue cells, such as fat, hematopoietic, liver, and brain cells, indicates that at times nonneoplastic cells can and do enter vascular channels. Since normal tissue cells, with the exception of trophoblastic cells, lack invasive properties of their own, it seems reasonable to assume that they enter vascular channels through defects in the wall caused by some extrinsic agent. With the exception of fat cell embolization in burns and of trophoblastic embolization in pregnancy, the embolization of normal tissue cells is usually associated with traumatic laceration of the tissue concerned, i.e., the occurrence of fat cell embolism that follows a bone fracture. The extravasation of blood through torn vascular channels results in an increase in the extravascular pressure at the fracture site. Thus, a situation is provided for the intravasation of fat cells through defects in the torn vascular channels if the extravascular pressure eventually exceeds the intravascular pressure.

Therefore, any set of circumstances which results in (1) defects in the wall of vascular channels and (2) an increase in the extravascular pressure above that of the intravascular would set the stage for a mechanical intravasation of cancer cells and, in some instances, normal tissue cells into vascular channels.

A naturally occurring set of circumstances may take place during the second and third stages of labor, at any time after the membranes have ruptured, and more especially after the separation of the placenta. At that time there is the possibility that amniotic fluid may intravasate into the torn venous sinuses at the placental site of the uterus.

An iatrogenic set of circumstances may set the stage for the mechanical intravasation of radiopaque media, air, or cancer cells during curettage. A uterovenous or uterolymphatic intravasation of radiopaque media has been observed during diagnostic hysterosalpingography. Drukman and Rozin reported 62 such cases in 2,000 hysterograms. They noted that the intravasation occurred more frequently after curettage or menstruation.

Similar examples have been reported by Sampson (15, 16) who, in surgical speci-

mens, injected the uterine cavity with mixtures of gelatin and radiopaque substances to study the shape of the uterine cavity and the possible reflux of dye through the fallopian tubes. After injection of one of his specimens, radiopaque material escaped from the severed uterine and ovarian veins. It was then found that simulated curettage prior to injection resulted in entrance of the radiopaque material into the veins of the uterus on every occasion. Sampson described the uterus as a venous sponge having two cavities—the uterine cavity proper and the venous cavity. If the endometrium were disrupted, these two cavities became contiguous, enabling foreign material to enter the veins if the uterine wall was relaxed and the pressure within the uterine cavity was greater than that in the venous sinuses.

Air embolism from the uterus, although usually thought of as a complication of criminal abortion, may occur during diagnostic insufflation of the uterus and tubes, especially after curettage or menstruation.

Since the disruption of the endometrium and, consequently, of numerous venous sinuses during curettage may result in the uterine cavity and these sinuses becoming contiguous, it would seem likely that an intravasation of cancer cells into the disrupted venous sinuses could occur in a similar manner to the radiopaque media or air.

The cancer cells isolated from the blood stream during curettage gained entrance as a result of (1) venous invasion with dislodgment during curettage, (2) a mechanical intravasation into disrupted venous sinuses, or (3) a combination of both routes. Venous invasion was noted in only 1 of the 4 patients in whom a shower of cancer cells was demonstrated in the blood stream during curettage.

Less is known about the transportation phase of the vascular dissemination of cancer because of technical difficulties in the isolation and identification of the relatively few cancer cells from the numerous formed elements of whole blood.

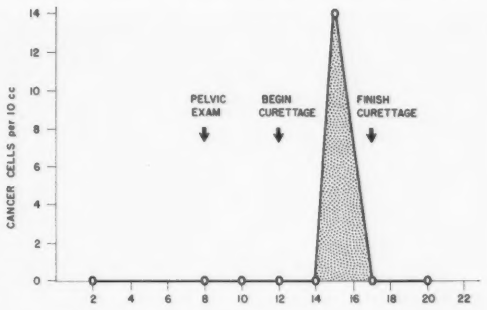
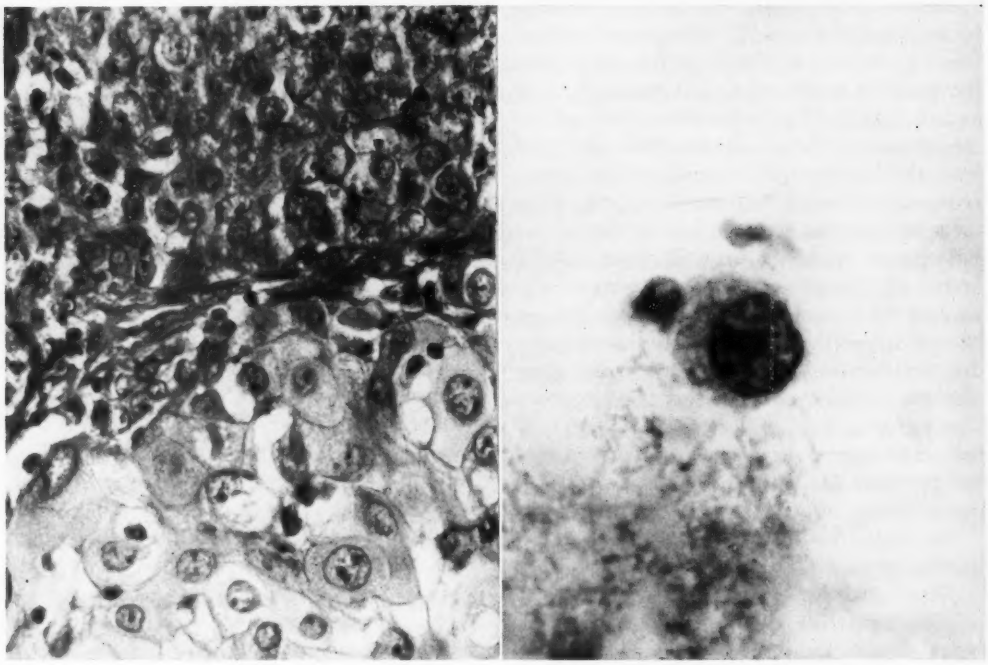


FIG. 5. Case 6. Cancer cells in the inferior vena cava during dilatation and curettage. The histologic diagnosis of this patient was adenoacanthoma of the uterus.

Recently, better methods have become available to isolate cancer cells. By utilizing Papanicolaou's methods of preservation and staining and criteria of malignancy, it is possible to show the similarity of cancer cells isolated from the blood stream to those obtained directly from a smear of the resected tumor, thus clearly confirming their malignant nature (Fig. 2).

In our laboratory, showers of cancer cells have been isolated from the circulating blood during such forms of manipulation as soap and water skin preparation for operation, attempted application of a renal pedicle clamp, mobilization of a malignant tumor, and transurethral resection of bladder and prostatic carcinoma. The need for frequent blood samples to detect an isolated shower of cancer cells is especially evident in Case 6 (Fig. 5.) in which cancer cells were found only in the blood sample drawn during the 30 second period that gritty tissue was encountered during curettage. The 5 blood samples taken prior to and the 2 blood samples taken after this period were negative for cancer cells.

The fate and therefore the significance of cancer cells in the blood stream during curettage is not known at this time. Many cancer cells are undoubtedly killed by host resistance. On the basis of autopsy and experimental data, Willis concluded that tumor embolism is not metastasis, a principle first stated by Goldman in 1897. In a study



a b

FIG. 6. Case 6. a, Tissue section, ×600, of curettage material from a patient with adenoacanthoma of the uterus. b, Cancer cell isolated from the inferior vena cava during curettage. Papanicolaou stain, ×1100. An erythrocyte is seen just to the left of the cancer cell.

of autopsy material, Schmidt has shown that many tumor emboli transported in the blood stream to the lungs die within vascular channels and therefore do not give rise to metastatic growths. The failure to establish metastasis may be related to the insecure attachment of the tumor emboli to the endothelium and lack of the formation of a surrounding thrombus, as emphasized by Schmidt and more recently by Wood who studied serial cinephotomicrographic records of vascularized ear chambers in rabbits.

Not all cancer cells perish within vascular channels; some cancer cells manage to survive and establish a metastasis. That this survival and establishment of metastases occurs in 10 to 15 per cent of patients with endometrial carcinoma is based on the reported incidence of pulmonary metastases in these patients. The successful establishment of a blood-borne metastasis depends on many factors, one of the most important of which is the viability of the cancer cells in transit in the blood stream. The viability of some human cancer cells isolated from the blood stream has been shown by Moore and his associates who were able to grow human melanoma and breast cancer cells in tissue culture. Jonasson (8) was successful in transplanting cancer in animals by injecting either whole blood or cancer cells isolated from the blood of sarcoma-bearing mice into normal mice with resultant tumor growth.

The important factor of time will help to clarify the fate of cancer cells in the blood stream during curettage. The over-all 5 year survival rate of 11,291 patients with endometrial carcinoma was 56.5 per cent (Table II) in an annual report published in 1958 (2). Since curettage was performed in all patients included in this report, the possi-

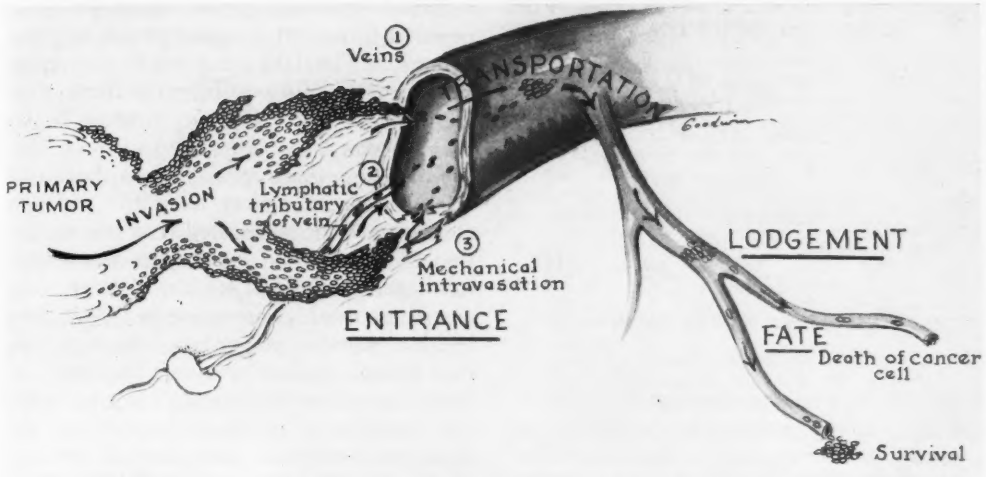


FIG. 7. Diagrammatic representation of sequence of events for the dissemination of cancer by vascular channels.

ble dissemination of cancer cells by any route—vascular channels, lymphatic channels, or fallopian tubes—could be significant in not more than 30 to 40 per cent of stage I cases on the basis of 5 year survivals. The patients reported herein were studied during the past 14 months and therefore must be followed up longer to determine the fate of the cancer cells.

The demonstration of cancer cells in the blood stream during curettage has certain clinical implications which are worthy of discussion. There is general agreement with the principle that cytologic evidence of malignancy should be confirmed histopathologically whenever possible prior to initiation of treatment. The accessibility of the uterine fundus to tissue examination by curettage has made it possible to adhere to this principle in the diagnostic evaluation of patients thought to have endometrial carcinoma. However, there are instances in which curettage may prove to be negative in spite of repeated positive cytologic reports. In some such cases, the curet has missed the neoplasm, or the neoplasm is located outside the uterine cavity, e.g., in the tubes, ovaries, or elsewhere in the peritoneal cavity. Conclusive cytologic evidence should not be ignored; it is an indication to the clinician that a meticulous and detailed search must be made for the source of the malignant cells recognized by the cytologist.

The inaccessibility of certain organs such as the lung to biopsy has made it impossible to adhere always to the principle of histopathologic confirmation. The cytologic method has become established as a reliable diagnostic procedure in the evaluation of the patient thought to have lung cancer. Day has stated that ". . . in effect, cytology has replaced histology as the major aid to the diagnostician and surgeon in the preoperative evaluation of lung tumors." Thus, in the management of a patient with clinical and roentgenographic manifestations of lung cancer but a normal bronchoscopic examination, Ackerman and Butcher, Spjut and associates, and others have considered preoperative conclusive cytologic evidence of malignancy as valid by itself, with a high degree of accuracy, and have recommended proceeding with definitive therapy without benefit of histopathologic confirmation by frozen section, to avoid possible spread of cancer cells.

This concept may also have application in the management of a patient thought to

TABLE II.—FIVE YEAR RESULTS OF TREATMENT OF CARCINOMA OF THE CORPUS

	No. of patients treated	*Alive with no evidence of disease*	*Relative apparent recovery rate, per cent*
Stage I (growth confined to uterus)			
Group 1 (operation advisable)	6,157	4,417	71.7
Group 2 (bad operative risk)	3,532	1,609	45.6
Stage II (growth spread outside uterus)	1,602	350	21.8
	11,291	6,376	56.5

Summary from *Annual Report on the Results of Treatment in Carcinoma of the Uterus* (2).

have endometrial carcinoma. The discussion should not, however, be considered as a condemnation of uterine curettage. Indeed, without histopathologic evidence the surgeon might possibly perform a needless operation and thus be guilty of a serious error, especially in the absence of convincing clinical manifestations of endometrial carcinoma and with cytologic evidence which is less than conclusive. He must weigh carefully all existing evidence, clinical, pathologic, and cytologic. In treating a postmenopausal patient with uterine bleeding and a normal cervix, the clinician is confronted with two possibilities when the cytologic evidence is conclusive for malignancy, i.e., class V.

First, without curettage, there is a possibility of not finding a malignant lesion in the resected uterus, as a result of proceeding with a radical surgical procedure on the basis of: (1) clinical manifestations of endometrial carcinoma; (2) a normal cervix; (3) a class V cytologic report which has been repeated; but (4) omitting curettage for confirmation. This possibility will be in direct proportion to the number of false positive cytologic reports.

Secondly, with curettage, there is a possibility, which has previously been thought to be theoretic, of disseminating cancer cells by vascular channels as a result of proceeding with a radical surgical procedure on the basis of (1) clinical manifestations of endometrial carcinoma; (2) a normal cervix; (3) a class V cytologic report which has been repeated; and (4) with curettage for confirmation. The data presented in this report suggest that this possibility is more than theoretic. Novak took issue with the advice of Sampson in 1924 (16) to avoid preliminary curettage except when there was no suspicion of cancer or if the patient's condition contraindicated radical operation. However, Novak stated that "certainly there is at least some evidence to suggest that possibly curettage in cancer, like incision into a malignant breast tumor, may lessen a patient's chances for cure . . . . There are, however, certain cases in which the omission of curettage is justified; for example, persistent and perhaps profuse uterine bleeding in women well beyond the menopause." Even though the entrance of cancer cells into the blood stream during curettage and the subsequent fate of these cells cannot be predicted in any particular patient, it could be significant in the 10 to 15 per cent of patients in whom pulmonary metastases are known to occur. As far as we are aware, there are no statistically valid reports in the literature, i.e., by a random sequence method, comparing the survival of patients with endometrial carcinoma who had diagnostic curettage prior to initiation of treatment with the survival of patients in whom treatment was carried out without a curettage.

The small number of cases included in this preliminary report precludes any statistical analysis, but they demonstrate that curettage can result in showers of cancer cells in the circulating blood. Although the fate of cancer cells demonstrated in the blood stream during curettage is not known at this time, "seeds" which are never sown on distant "soils" cannot grow there.

SUMMARY AND CONCLUSIONS

Ten patients with various malignant and benign diseases of the uterus were studied during uterine curettage by serial blood samples which were drawn at frequent intervals before, during, and after curettage.

The presence or absence of cancer cells in each blood sample was subsequently determined.

No abnormal cells were isolated from the blood of the 3 patients with benign diseases or the 2 patients with epidermoid carcinoma or carcinoma in situ of the cervix uteri.

Cancer cells were isolated from blood samples drawn during curettage from 4 of the 5 patients with malignant diseases involving the endometrium. In 3 of these cases the cancer cells were demonstrated only during curettage—none before or within minutes afterward.

Whether the entrance of cancer cells isolated during curettage was the result of a dislodgment of cancer cells which had invaded uterine veins or a mechanical intravasation into disrupted venous sinuses is not known.

From the data reported herein it is concluded that the vascular dissemination of cancer cells during curettage is more than a theoretic possibility in patients with malignant diseases involving the endometrium.

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EXPERIENCES IN THE MANAGEMENT OF 150 CONSECUTIVE CASES OF MASSIVE UPPER GASTROINTESTINAL BLEEDING

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THIS REPORT reflects an experience with a program of management which was inaugurated in 1952 at the Beekman-Downtown Hospital in an effort to cope better with the problem of acute severe upper gastrointestinal bleeding as it is encountered at that emergency clinic. The distinctive features of this experience with 150 such patients admitted between 1 January 1952 and 31 December 1958, are: (1) Every patient was admitted as an emergency case via our ambulance service. (2) Each patient was admitted directly to our Surgical Service. (3) At the time of admission, the patients were personally evaluated by the authors who have served as a team in supervising their care.

In presenting this report of a controlled select experience, it is not our purpose to advocate a particular policy but, rather, to direct attention to an important consideration in interpreting a clinic's experience with acute upper gastrointestinal hemorrhage, namely, the circumstances under which the problem is encountered. These circumstances have long been impressed upon us by the contrast between experiences while being associated concurrently with an emergency hospital with an active ambulance service and with two large general hospitals without such facilities. This contrast is reflected in distinctive differences in the nature of the clinical material and in problems of diagnosis and management. This perspective is well illustrated by the following quotation from a recent report on massive bleeding in duodenal ulcer by Gardner and Baronofsky: "Admission to Mount Sinai Hospital, New York City is almost invariably on an ambulatory basis. Occasionally a private ambulance is employed to transport a patient to the hospital for admission, but there is no ambulance service associated with the hospital. The patient who has time to go to his private physician with a complaint of tarry stools and is then referred to the hospital for admission is far different from the patient who faints after a massive hematemesis and is brought to the hospital by ambulance."

The Beekman-Downtown Hospital, located in lower Manhattan, New York, serves as an emergency hospital to a large nonresidential area devoted to financial, industrial, and governmental activities. It is estimated that a million persons enter and leave this area during the working day. This transient population reflects most varied economic, social, and geographic backgrounds—including the financial executive, the white collar and civil service worker, the laborer, the tourist, and the migratory derelict and chronic alcoholic from the Bowery section of New York. When an acute emergent condition occurs in one of this transient group, the victim, as a rule, is brought to our hospital by our ambulance service. Rarely is the problem of acute severe upper gastrointestinal bleeding encountered under circumstances when helpful information is made available by a family physician or by accessible hospital records. Although it had been the practice to admit all such patients, regardless of

From the Surgical Service, Beekman-Downtown Hospital, New York.

severity, to our medical service, the logicality of this arrangement always remained open to question. To some, it seems more reasonable to place patients with acute serious bleeding presenting an imminent need for surgical intervention under the direct observation of those who are to carry out such care. In 1952, this latter point of view was generally accepted. Accordingly, the policy of admitting all patients with acute upper gastrointestinal bleeding to our Surgical Service and under our direct supervision was initiated.

Between 1 January 1952 and 31 December 1958, 248 patients were admitted to the Surgical Service because of sudden hematemesis, melena, or both. In 150 of these, the bleeding was classified as massive on the basis of its evident severity and the patient's disturbed physiologic reaction to blood loss. This evaluation was made to a large extent on clinical grounds and only secondarily on the basis of laboratory data, which is often unreliable as an indicator of the extent of blood loss. The term massive is most difficult to define precisely. It may be said that in all of these 150 cases a strong possibility of rapid, fatal bleeding was suggested. When laboratory data were obtained after some degree of physiologic adjustment, in every case the hemoglobin level was 8.5 grams or less, the red blood count was 3 million or less, and the hematocrit was 30 or below. The minimal amount of blood replacement to establish physiologic stabilization in any single case was 1,500 cubic centimeters.

The following program, as a rule, is promptly started in our emergency room: (1) At the time of admission each patient is evaluated by a member of the team to determine the severity of the bleeding and to establish a base line upon which to judge subsequent clinical behavior. (2) Measures are immediately instituted to combat shock and anoxemia by adequate and judicious blood replacement such as gelatin or dextran until blood becomes available. (3) Concomitant with the use of supportive measures, a formal diagnostic program is carried out to confirm the existence of an upper gastrointestinal hemorrhage and to determine its cause.

TABLE I.—CAUSES OF SEVERE UPPER GASTROINTESTINAL BLEEDING IN 150 CASES

		Management	
Diagnosis	*No.*	*Surgical*	*Nonsurgical*
Duodenal ulcer	61	34	27
Gastric ulcer	24	18	6
Gastrojejunal ulcer	7	4	3
Esophageal varices	23	0	23
Acute gastritis	12	0	12
Undetermined	15	0	15
Leiomyosarcoma	3	2	1
Uremia	2	0	2
Carcinoma	2	1	1
Strongyloides	1	0	1
	150	59	91

At the outset a Levin tube is passed. If blood is obtained, the diagnosis of an upper gastrointestinal hemorrhage is confirmed. With the tube left in situ for 24 to 48 hours, the gastric drainage serves as an indicator of the continuance, arrest, or recurrence of bleeding.

With the admission of a transient unknown patient, a searching clinical history and a careful physical examination have proved most rewarding in establishing the cause of the bleeding. In eliciting the history, particular attention is paid to the possible factors of alcoholism and drugs. When the diagnosis of peptic ulcer is evident or suspected, much significance is given to the presence or absence of pain.

Since the feasibility of the surgical control of bleeding is limited almost solely to peptic ulceration, our major aim is promptly to distinguish that condition from other less common causes, such as bleeding esophageal varices and blood dyscrasias. Endoscopy has rarely been employed. Roentgenologic examination is not performed in the presence of shock and active bleeding but an open mind is maintained about its use within the first 24 to 48 hours after bleeding has apparently stopped, in cases of uncertain diagnosis. The finding of a gastric ulcer, because of its greater inherent danger, is an important factor inducing prompt surgical intervention. In 15 cases in which emergency roentgenologic examination was

TABLE II.—CORRELATION OF PATHOLOGY WITH CLINICAL MANIFESTATIONS (THERAPEUTIC GUIDE)

Probable pathology	*Probable caliber of bleeding vessel*	*Likely bleeding manifestation*	*Likely significant associated symptoms*	*Likely response to blood replacement (therapeutic test)*	*Advisability of surgical intervention*
Chronic calloused penetrating ulcer	D.U.—Branch of gastroduodenal artery	Exsanguinating or continuous unstabilized	Pain, hematemesis	Unfavorable	Prompt
	G.U.—Branch of left gastric artery		Pain, hematemesis	Unfavorable	Prompt
Chronic ulcer non-penetrating	D.U.—Small	Severe	Pain, hematemesis	D.U.—Favorable	Prompt for (1) Recurrence after temporary stabilization (2) Continuous after 24 to 48 hours
	G.U.—Larger and more numerous	Continuous unstabilized	Pain, hematemesis	G.U.—Unfavorable	
Superficial ulcerations	D.U.—Small	Moderate to severe	Mild or absent	D.U.—Favorable	Deferred unless uncontrolled
	G.U.—Microscopic			G.U.—Favorable	
Erosions	D.U.—Microscopic	Moderate to severe	Mild or absent	D.U.—Favorable	Deferred unless uncontrolled
	G.U.—Multiple			G.U.—Favorable	
Diffuse gastritis	Diffuse microscopic	Moderate to severe	Mild or absent	Favorable	Deferred unless uncontrolled

D.U., duodenal ulcer; G.U., gastric ulcer.

performed, it proved helpful in 8 cases, uninformative in 4 cases, and misleading in 3 cases.

The diagnoses made are summarized in Table I. It is to be noted that in 92 instances or 61 per cent of the cases, the cause of bleeding was attributed to peptic ulceration, and in 15 cases or 10 per cent the cause was undetermined. All of these latter patients had a complete gastrointestinal investigation including esophagoscopy and sigmoidoscopy with no apparent disease discernible. It is conceivable that some of the patients in the undetermined group may have bled from superficial erosions in the stomach or duodenum, which were not demonstrated by roentgenologic examination.

There were 12 patients who bled profusely in whom a large alcoholic intake could readily be ascribed to be the cause. These patients, for the most part, were chronic alcoholics. While most patients with alcoholic gastritis as a rule do not bleed severely, however, when they do, they may present a trying diagnostic problem. There were no deaths in this series.

There were 23 patients with severe hematemesis which was proved to be caused by esophageal varices. The diagnosis for the most part was readily made by the clinical history of chronic alcoholism, the stigmas of cirrhosis, and the confirmatory evidence of temporary arrest of the bleeding by the Sengstaken tube. Nearly all of these patients were of the derelict type, in poor physiologic condition from the effects of liver disease, avitaminosis, and malnutrition. All these patients were treated by the Sengstaken tube and blood replacement during acute bleeding, with the hope for an arrest of hemorrhage and eventual definitive surgery in an interval phase. Sixteen of them died, either from a recurrent hemorrhage or from hepatic insufficiency.

Our therapeutic policy is one of evaluating each case as an individual problem, favoring selective surgical intervention under certain specific conditions rather than routine exploration. In assaying the individual case, much significance is ascribed to pain as an indicator of the prevailing pathologic condition—which is a prime factor in determining the persistence of bleeding and its response to medical measures.

This perspective was first impressed on Ginzburg and Mage (2) in a study of patients with bleeding gastrojejunal ulcers following gastroenterostomy, who had been subjected to partial gastrectomy. In the instances of painless bleeding, the specimens revealed superficial ulcerations with no

TABLE III.—PROCEDURES USED IN 150 CASES OF ACUTE SEVERE UPPER GASTROINTESTINAL HEMORRHAGE

	No. of cases	*No. of deaths*
Emergent procedures	41	
Subtotal gastrectomy	35	
Duodenal ulcer	21	3
Gastric ulcer	13	2
Leiomyosarcoma	1	0
Exploration only	3	
Carcinoma	1	1
Leiomyosarcoma	1	0
Gastric ulcer	1	1
Suture ligation—marginal ulcer	2	0
Local excision—gastric ulcer	1	0
Interval procedures—same admission	18	
Subtotal gastrectomy	18	
Duodenal ulcer	13	0
Gastric ulcer	3	0
Gastrojejunal ulcer	2	0
Total	59	7

TABLE IV.—EMERGENT SUBTOTAL GASTRECTOMY FOR BLEEDING ULCERS

	Duodenal ulcer		*Gastric ulcer*		*Total*		*Pathology*
	No.	*Deaths*	*No.*	*Deaths*	*No.*	*Deaths*	
Exsanguinating	3	1	2	0	5	1	Penetrating ulcers with open vessel
Recurrent—nonstabilizing	13	1	5	0	18	1	10 penetrating ulcers with open vessels 8 craters, no open vessel
Continuous	5	1	6	2	11	3	9 nonpenetrating ulcers 2 multiple superficial gastric ulcers
Total	21	3	13	2	34	5	

tendency to impinge on adjacent vessels. In the cases of bleeding associated with pain, the ulcers were found to be deep and actively penetrating. These observations have been confirmed in several similar subsequent studies relating to peptic ulcer in general (3, 4). As noted in Table II, these observations have been translated into a therapeutic guide.

When massive bleeding is associated with pain, we are prepared to operate early as in all probability a vessel of such caliber has been compromised by an active penetrating ulcer, and a favorable response to conservative measures would be unlikely or impossible.

We tend to treat painless bleeding conservatively since a superficial lesion probably exists and, therefore, a favorable response is likely. There were 15 cases (11 duodenal and 4 gastric ulcers) proved by roentgenology or operation in which no history of pain could be elicited. It is significant that in the duodenal cases melena was the sole symptom. The bleeding stopped spontaneously in 12 of these 15 cases. Three patients were subjected to prompt operation because of the severity and the persistence of the bleeding. In each instance, multiple superficial ulcerations proved to be responsible. Death resulted in 1 of these cases from continued bleeding from multiple erosions remaining in the gastric stump. This type of case may fall in the category which Mixter and his associates have recently claimed may be best treated by vagotomy.

Another most important consideration influencing the decision to operate early is the patient's likely intolerance of prolonged anoxemia, judged by such factors as age and associated degenerative diseases. The more promptly such patients are operated upon, the better is the chance for survival.

In the light of these considerations, emergent operation was used in 41 of the 150 patients with acute upper gastrointestinal hemorrhage (Table III). In 3 instances, the bleeding resulted from causes other than peptic ulceration, e.g., leiomyosarcoma in 2 cases and carcinoma in 1 case. Thus of 92 cases of massive bleeding peptic ulceration, 38 patients were operated upon emergently, and 54 patients were treated conservatively. Although indicated, surgery was not resorted to in 6 cases, either because of the patients' refusal or because of physical status. Forty-eight patients were managed conservatively because they remained stabilized

TABLE V.—SIX DEATHS IN 38 PATIENTS WITH BLEEDING ULCERS TREATED BY EMERGENT OPERATION

Name, Age, years	*Duration of bleeding prior to surgery*	*Pathology at surgery*	*Operation*	*Cause of death*
R.K. 58	24 hrs. persistent	Penetrating duodenal ulcer (open vessel)	S.T.G.	P.M. Hepatic necrosis 96 hrs. p.o.
E.W. 57	24 hrs. persistent	Chronic duodenal ulcer	S.T.G.	Cardiac arrest
J.M. 48	3rd recurrence on 15th hospital day	Chronic duodenal ulcer	S.T.G.	P.M. Strangulated efferent loop obstruction 19th p.o. day
J.B. 58	Periodic recurrence for 13 days	None found	Exp. lap.	P.M. Bleeding high gastric ulcer. 48 hrs. p.o.
F.S. 56	7 days—persistent	Gastric ulcer (lesser curv.)	S.T.G.	P.M. Peritonitis 96 hrs. p.o.
E.B. 55	48 hrs. persistent	Multiple gastric ulcers, acute gastritis	S.T.G.	P.M. Hemorrhage 72 hrs. p.o. Acute gastritis with superf. ulcers, gastric stump

S.T.G., subtotal gastrectomy.

after blood replacement. Thirty-four of this latter group would have been operated upon promptly if bleeding had recurred. Actually, interval partial gastrectomy before discharge from the hospital was advised for 34 of these patients. Eighteen accepted such surgery within a period of 10 to 21 days after stabilization. There was no mortality in this group. At operation, chronic or healed ulcers were revealed in all these cases. This experience has modified our previously held attitude concerning the advisability of delaying operation after massive bleeding for periods as long as 3 months in order to obtain complete physiologic recovery.

Table IV is a breakdown of the 34 cases in which emergent operation was performed. In 5 instances the bleeding was of such intensity as to be actually exsanguinating despite the amount and rapidity of blood replacement. In such cases there is no alternative but prompt surgical intervention even if the diagnosis of ulcer is only suggestive. These 5 patients were subjected to subtotal gastrectomy within 6 hours of admission with 1 fatality 96 hours after operation from liver necrosis. All these patients had long-standing histories of chronic ulcer disease with pain being an outstanding symptom. In addition, all had frank hematemesis. At operation, in every instance, either a chronic penetrating duodenal or gastric ulcer, with an open pumping vessel, existed. It is believed that 4 of these patients were salvaged by prompt operation.

When bleeding is severe but not exsanguinating, each patient has been given a chance for physiologic stabilization by prompt blood replacement of 500 cubic centimeters every hour until a total of 1,500 cubic centimeters has been given. In the event that this objective is obtained and bleeding subsequently recurs, operation is resorted to promptly in the patient with a history of chronic ulcer in which pain and hematemesis are prominent symptoms, particularly, if the patient is in an older age group or if there is evidence of associated degenerative disease. Eighteen emergent subtotal gastrectomies were performed for recurrence of severe bleeding; 17 after 24 to 72 hours of stabilization and 1 after 21 days. There was 1 death from an efferent loop obstruction 14 days after operation. It is to be noted that all these patients experienced frank hematemesis. In 10 instances in which severe pain preceded or occurred at the time of bleeding, chronic calloused penetrating ulcers with open vessels were found. In 8 cases in which the factor of pain was not striking, operation revealed chronic nonpenetrating ulcers with no evident bleeding vessel.

The third situation in which surgical intervention was resorted to, unfortunately at times with not sufficient promptness, was that of a continuous substantial bleeding in which as much as 1,500 cubic centimeters of blood were administered daily to maintain a satisfactory blood volume. This type of bleeding is the most insidious and, in some

respects, most dangerous. There is a tendency to temporize as the patient appears to be stabilized. If such bleeding is permitted to continue in a patient, who may tolerate the effects of prolonged anoxemia poorly, rapid physiologic deterioration suddenly occurs. The timing of operation is most important. Operating within 24 to 48 hours is favored if bleeding has not stopped, particularly if a gastric ulcer exists. There were 11 patients in this group who were subjected to subtotal gastrectomy after 3 to 6 days of continued bleeding (Table IV). In 9 cases nonpenetrating chronic ulcers (5 duodenal and 4 gastric) were found, and in 2 cases multiple superficial gastric ulcers. Three deaths in this group were caused by (1) cardiac arrest shortly after termination of the procedure, (2) exsanguinating bleeding from erosions in the gastric stump 3 days after resection, and (3) peritonitis with no evidence of disruption of the duodenal stump or gastroenteric anastomosis at autopsy.

A tabulation of the deaths from conservative therapy and emergent surgery are noted in Tables V and VI.

As far as the operative procedure is concerned, a subtotal gastrectomy with the removal or the exclusion of the ulcer site from the gastrointestinal tract is considered to be the most certain means of controlling hemorrhage. In rare instances in which the general condition of the patient or the local pathologic condition precludes a gastric resection, less satisfactory measures have been resorted to, such as suture ligation of the bleeding site or local excision of the ulcer. These procedures were carried out in 3 instances with satisfaction. When exploration fails to reveal the pathologic condition an empiric subtotal gastrectomy is performed and the proximal end of the stomach is carefully inspected for bleeding from a retained peptic ulcer or from gastric varices. In 3 instances in which empiric gastrectomies were carried out, the resected specimens revealed superficial gastric ulcers to account for the severe bleeding. An exploratory gastrotomy or duodenotomy is not performed unless the stomach is obviously distended with blood.

TABLE VI.—SIX DEATHS IN 54 PATIENTS WITH BLEEDING ULCERS TREATED CONSERVATIVELY

Name Age, yrs.	*Duration of bleeding*	*Reasons for medical therapy*	*Cause of death*
S.K. 50	6 days—persistent	Alcoholic cardiac failure, pneumonitis	P.M. Hemorrhage from penetrating duod. ulcer. Bronchopneumonia
V.G. 60	24 hrs. exsanguinating	Refused surgery	Died in 24 hrs. No P.M. Hemorrhage
R.S. 81	24 hrs. exsanguinating	Severe cardiac. Never in condition for surgery	P.M. Hemorrhage. Large gastric ulcer
J.J. 43	48 hrs. recurrent exsanguinating	No ulcer symptoms. Previous sympathectomy for hypertension	P.M. Hemorrhage. Large gastric ulcer
W.F. 54	24 hrs. exsanguinating Hgb. 3.3 gm.	Coma. No diagnosis	Hemorrhage. No P.M.
C.M. 49	5 hrs. exsanguinating Hgb. 4.7 gm.	Terminal state	Hemorrhage. No P.M.

In the instance of a patient with an uncontrollable exsanguinating bleeding, operation should not be deferred until a certain hemoglobin level is attained or a shock-like state is corrected. In such a case, the ulcer site should be promptly exposed with control of the bleeding vessel by a suture ligation. This is not always readily accomplished, but more success has been attained with a figure of 8 suture ligature directly over a tab of gelfoam. With the bleeding so controlled, the patient's condition frequently can then be restored by blood replacement to permit indicated further surgical procedures.

SUMMARY

It is not possible to generalize with certainty as to whether it is preferable to admit patients with acute upper gastrointestinal bleeding to the medical or surgical services, or as to which supervisory arrangement may provide the most efficient management.

Much depends on the circumstances prevailing in any individual clinic and, particularly, on the availability and application of those involved in any team arrangement. However, in an emergency clinic such as ours, it seems more reasonable to admit patients with acute serious bleeding to the surgical service.

It is well recognized that certain patients with peptic ulcer may succumb to hemorrhage despite all therapeutic efforts. It is quite evident from empiric experience that some of these patients may be saved by well-timed and proper surgery. On the basis of the existing pathology, this was the case in 4 out of 5 patients with exsanguinating bleeding and in 10 of the 18 with severe recurrent bleeding.

Two deaths resulted from surgical complications, e.g., cardiac arrest and efferent loop obstruction, in patients who conceivably might have recovered from the hemorrhages without surgical intervention. These facts emphasize that the inherent risks of operation cannot be overlooked in considering its use. It is for this reason that a policy of selective intervention by evaluating each case as an individual problem is favored, rather than one of routine surgical intervention under certain specific conditions, as advocated by some.

Upon the basis of this experience we believe that a patient with chronic peptic ulceration, whose condition becomes stabilized after serious bleeding, may be safely subjected to interval surgery sooner than was previously thought.

A correlation between the clinical manifestations of pain and the probable prevailing pathology has been found to be a serviceable therapeutic guide.

We believe our results with the treatment of bleeding peptic ulceration to be reasonably satisfactory, but since no acceptable basis for comparison exists it is impossible to evaluate them with the experience of others.

Our results with the treatment of bleeding varices remain frustrating and depressing, mainly because of the clinical material with which we are confronted.

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THE DEVELOPMENT OF CLEFT PALATE RESULTING FROM MATERNAL PTEROYLGLUTAMIC (FOLIC) ACID DEFICIENCY DURING THE LATTER HALF OF GESTATION IN RATS

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UNTIL RECENTLY defects in the development of the palate were attributed almost entirely to genetic factors. It is only within the past two decades that experimental procedures applied to the maternal organism have produced cleft palate, as well as many other congenital defects, in the young of mammals. The review of Kalter and Warkany (6) of metabolic alterations which result in congenital malformations shows that cleft palate may result from the following changes in the maternal environment: nutritional deficiencies (vitamin A, riboflavin, folic or pteroylglutamic acid, pantothenic acid, niacin, vitamin E, and fasting), hypervitaminosis A, endocrine disturbances (hypothyroidism, cortisone injections), hypoxia, hypothermia, and injection of trypan blue, or of nitrogen mustard and other alkylating agents. Nishimura and colleagues (9–11) have reported cleft palate following injection of equine serum gonadotropin, ethylurethan, and nicotine. The defect also follows x-irradiation, as was shown by Warkany and Schraffenberger (18) and Wilson. In fact, cleft palate is one of the anomalies most commonly encountered in experimental teratology. It has even been observed in human fetuses following administration of a folic acid antimetabolite, aminopterin, as indicated by Thiersch and Warkany and associates (17).

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In many of these experimental circumstances, however, cleft palate was encountered only sporadically or in low incidence. In order that the sequence of faulty development may be reconstructed, it is necessary that the experimental procedure yield a very high incidence of the anomaly in newborn animals. Only then may the earlier fetal stages of palate formation be examined with a reasonable expectation that they would ultimately be associated with palatal deformity. Three teratogenic procedures have been reported to result in a 90 to 100 per cent incidence of the deformity: hypervitaminosis A in rats reported by Giroud and Martinet, cortisone injections into cleft palate "susceptible" strains of mice by Fraser and associates and Kalter (3, 5), and pteroylglutamic acid (PGA) deficiency in rats of the Long-Evans strain (8). In the latter strain spontaneous occurrence of cleft palate has not been seen to our knowledge.

This report deals with the normal development of the palate and with faulty palatal morphogenesis in rat fetuses whose mothers had been subjected to a PGA deficiency throughout the latter half of pregnancy. Such a regimen resulted in a simple form of palatal defect associated with many other anomalies in the same young. Among these other anomalies, faulty development of the mandible was observed and has been analyzed in this study because of its possible relation to palatal development. A subsequent report will deal with the description and incidence of more bizarre and varied pala-

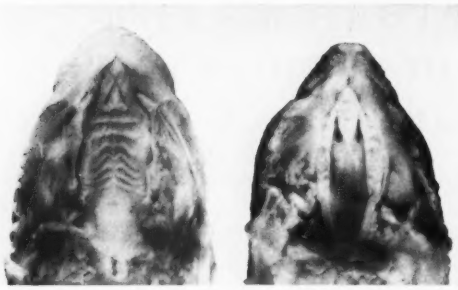

FIG. 1. Ventral aspect of palate in 21 day old rat fetuses. Left, Normal; right, PGA-deficient fetus (deficiency instituted on the eleventh day of pregnancy). The palatal gap is representative of the majority of fetuses in the PGA-deficient group. ×3.3.

tal, labial, nasal, and maxillofacial malformations encountered when a transitory PGA deficiency of 2 to 3 days was induced earlier in pregnancy.

MATERIALS AND METHODS

The experimental procedures have been described in detail previously (8). Normal rats of the Long-Evans strain were transferred on the tenth, eleventh twelfth or thirteenth day of pregnancy[1] to a PGA-deficient diet[2] containing succinyl sulfathiazole (SST) and a "crude" PGA-antagonist. Controls were maintained either on a stock diet[3] consisting of natural food sources in optimal proportions, or on a purified diet containing SST and a high level of the vitamin PGA.[2] The young were obtained on the twenty-first day of gestation, 12 to 24 hours before anticipated parturition. In the majority of cases, some young from each litter were fixed in Bouin's solution for histologic study; the remainder were fixed in 95 per cent alcohol for clearing and alizarin red S staining of the skeleton by a modified Spalteholz technique described previously (20).

In order to follow the stages of normal and abnormal development, young were obtained at one day intervals from the thirteenth to the twenty-first day from pregnant rats given the PGA-deficient or control diet from the eleventh day of gestation. Some control young were obtained at half-day intervals during the same period.

[1]The day of finding sperm in the vagina was considered to be day zero.

[2]The PGA-deficient diet was composed of 24 per cent alcohol-extracted casein, 62.5 per cent sucrose, 8 per cent hydrogenated cottonseed oil, 4 per cent salts No. 4, 1 per cent SST, and 0.5 per cent "crude" PGA-antagonist (x-methyl-PGA). Crystalline vitamins per kilogram of diet were: 300 mcgm. *d*-biotin, 5 mgm. 2-methyl-1,4-napthoquinone, 5 mgm. thiamine HCl, 5 mgm. pyridoxine HCl, 10 mgm. riboflavin, 10 mgm. p-aminobenzoic acid, 20 mgm. nicotinic acid, 50 mgm. *d*-calcium pantothenate, 400 mgm. inositol, and 1.0 gm. choline chloride. All rats received weekly a fat-soluble vitamin mixture containing 800 U. S. P. units vitamin A, 115 chick units vitamin D, 6 mgm. *dl*-alpha tocopherol, and 650 mgm. corn oil. Control animals were maintained on the identical diet supplemented with 50.5 mgm. synthetic PGA per kilogram diet.

[3]The stock diet used for pregnancy was composed of 67.5 per cent ground whole wheat, 15.0 per cent technical grade casein, 7.5 per cent skim milk powder, 6.75 per cent hydrogenated vegetable oil, 1.5 per cent calcium carbonate, 0.75 per cent iodized sodium chloride, and 1.0 per cent fish oil (vitamin A and D concentrate). Lettuce is given ad libitum twice weekly.

TABLE I.—INCIDENCE OF CLEFT PALATE AND HARELIP IN YOUNG FROM MOTHERS SUBMITTED TO PGA-DEFICIENCY DURING THE LATTER PART OF GESTATION

Deficiency period, days of gestation	*No. of young*	*Cleft palate, per cent*	*Harelip, per cent*
10–21	39	100	21
11–21	194	>95	0
12–21	109	<2	0
13–21	70	0	0

Adapted from Nelson, Asling, and Evans (8) and Nelson (7).

RESULTS

Incidence of cleft palate. Table I shows the incidence of palatal and labial defects encountered when pregnant rats were given the PGA-deficient diet from the tenth, eleventh, twelfth, or thirteenth day of gestation until the twenty-first day. Instituting the deficiency on the tenth day resulted in the invariable occurrence of cleft palate; one-fifth of the fetuses also had labial deformities. When the PGA-deficient diet was introduced on the eleventh day, a very high incidence of cleft palate was encountered in the young, but there were no appreciable labial deformities. Palatal abnormalities were very rare in fetuses from mothers deficient from the twelfth or thirteenth day of gestation. No anomalies were encountered in offspring from the control mothers.

Figure 1 illustrates the palate of a normal fetus and that of a PGA-deficient fetus whose palatal defect is representative of the majority of those from the 11 to 21 day group. The lateral palatine processes may

FIG. 2. Cleared, alizarin-stained heads of 21 day old rat fetuses showing ossification centers. Left, Normal; right, PGA-deficient. ×3.5. Diagrammatic line drawing.

be seen as narrow shelves but approximately three-quarters of the roof of the mouth is lacking. This appearance characterized 67 per cent of the fetuses in this group. In 22 per cent the gap occupied half of the roof of the mouth, and in 5 per cent it was reduced to one-quarter of the roof or less. Occasionally (1 per cent of the fetuses), the roof of the mouth was almost entirely lacking.

The bony defect is shown by the alizarin-stained cleared skulls in Figure 2. The defect involves the palatine processes of the maxillary bones and the horizontal processes of the palatines, thus allowing the vomer and presphenoid ossification center to be seen through the gap.

Development of normal and cleft palate. The process of palate formation in the rat has not been previously described in detail. In mice, Walker and Fraser (16) have provided a full account which included observations of the living fetus. Fraser (2) has commented on the similarity of palate formation in mice to the process described in man.

The gross appearance of the roof of the mouth in the normal rat at representative ages (14 to 17 days by half-day intervals) is shown by the series of diagrams in Figure 3. A general outline will assist in following the details of events shown here and in the subsequent histologic sections. The primitive nasobuccopharyngeal cavity becomes subdivided ultimately into four cavities (oral, paired nasal, and pharyngeal cavities). The oral cavity is separated from the nasal cavities by a pair of lateral palatine processes which, appearing first on the dorsolateral wall of the primitive cavity, grow ventromedially and later medially. Finally, they meet in the midline and thus form the palate. The downgrowth of a median nasal process from the roof of the primitive oral cavity divides the nasal region; this process fuses with the palate along the midline and comprises the definitive nasal septum. More caudally, these processes are not formed and the nasal and oral cavities are confluent in the pharyngeal cavity.

In the diagrams it will be noticed that the edges of the palatine shelves are not straight but instead follow a sinuous outline. They first join in the midline at a level between the commissures of the mouth and the rostral portion of the eye. These well-demarcated and significant landmarks were therefore used in selection of the histologic sections shown in Figures 4 to 22, which were all cut in the frontal plane passing through this level. The following account of normal and abnormal development refers both to diagrams and to histologic sections.

DAY 13. In the normal rat of this age the primitive oral cavity has already been divided into the mouth and a pair of short passages leading from the external

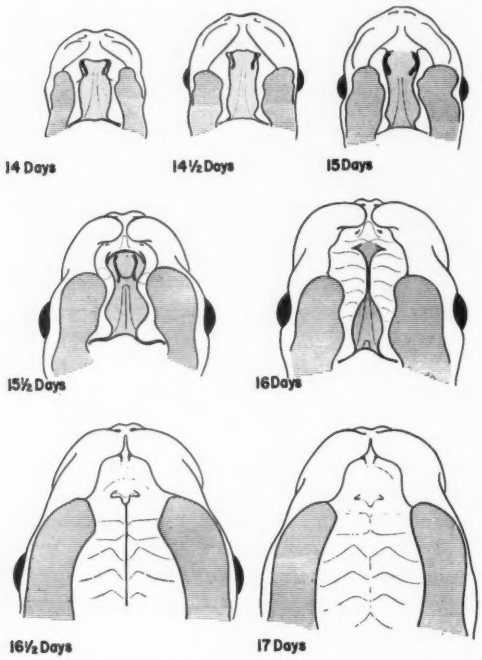

FIG. 3. Diagrams showing development of the palate in normal fetal rats from the fourteenth to the seventeenth day of gestation. Horizontal lines indicate cut surface resulting from removal of lower jaw. Stippling indicates nasal cavity.

nares to the primitive choanae. These latter passages are established between day 12½ and 13. Figure 4 shows a slight swelling on the buccal aspect of the maxillary process where the lateral palatine processes will arise. The paired dark circular regions dorsally are components of the telencephalon.

In the PGA-deficient fetus (Fig. 5) no appreciable structural difference can be seen from the control.

DAY 14. In the normal fetus a shelf, the premaxillary process, is growing back from the rostral end for the further separation of the nasal and oral cavities (diagram, Fig. 3 and cross-section, Fig. 6). Laterally the maxillary processes show prominent elevations, the lateral palatine processes. The free margins of these latter processes and of the premaxillary process join rostrally to make a deep rectangular fossa which is open caudally. In the roof of the cavity a well-defined longitudinal ridge is down-growing nasal septum.

In the PGA-deficient fetus (Fig. 7), structural development is still parallel to that of the control.

DAY 15. In the normal fetus, the premaxillary process has completed the most rapid phase of its caudad growth (diagram, Fig. 3), and henceforth grows only in pace with the general growth of the head. The lateral palatine processes are growing in a ventromedial direction, most rapidly in their anterior one-third. However, they have encountered the equally rapidly growing tongue arising from the floor of the mouth (Fig. 8). The tongue occupies not only the oral but also the lower portion of what will be the nasal cavity and lies almost in contact with the nasal septum. In cross-section the tongue is trapezoidal in shape. The lateral palatine processes are temporarily trapped below the lateral margin of the tongue. Condensation and beginning chondrification of the mesenchyme may be seen lateral to and above the nasal cavity and into its septum. Alizarin staining may show spicules of bone in the premaxilla.

In the PGA-deficient fetus (Fig. 9) the head is slightly smaller than normal, but the topographic relationships are like those in the control. The connective tissue in the nasal septum and lateral to the nasal cavity shows mesenchymal condensation but not chondrogenesis.

DAY 16. In the normal fetus, differential growth (including development of the lower jaw) has resulted in descent of the tongue from the nasal region. In cross-section it is becoming oval in form and it now occupies only the lower portion of the primitive oral cavity (Fig. 10). The freed lateral palatine processes are approaching each other medially. In order to do so the axis of their growth has shifted from the angling ventromedial direction to a horizontal plane.

Appreciable individual variation may be encountered at this stage, even within the same litter. It is possible to find the lateral palatine processes impinging upon each other in the midline for a short distance as early as 15½ days. On the other hand, they may be completely separated by a straight narrow slit as late as 16½ days. The diagram and histologic section illustrate the most commonly encountered state of development, i.e., nasopalatine contact without fusion and a midline palatine gap, narrow rostrally but widening toward the pharynx.

Embryonic heads cleared and stained *in toto* showed small vertical spicules of bone lateral to the nasal cavities, representing ossification centers in the maxillae and palatine bones. No bone was present in the palatal shelves. The premaxillary ossification center was expanding.

The rostral Y-shaped gap which remains at this age (Fig. 3, 16½ days) should be noted. A small elevation on the premaxillary process occupies the region between the upper limbs of the Y. The open area forms a temporary passage, the nasopalatine canal. At the caudal end of the fusion line of the palatine raphe a gap can be seen occasionally, V-shaped or slitlike depending on the stage of advancement. The oral and nasal cavities are confluent through this gap, and the tongue may still be interposed here.

In the 16 day PGA-deficient fetuses, abnormal development may now be observed after 5 days of ma-

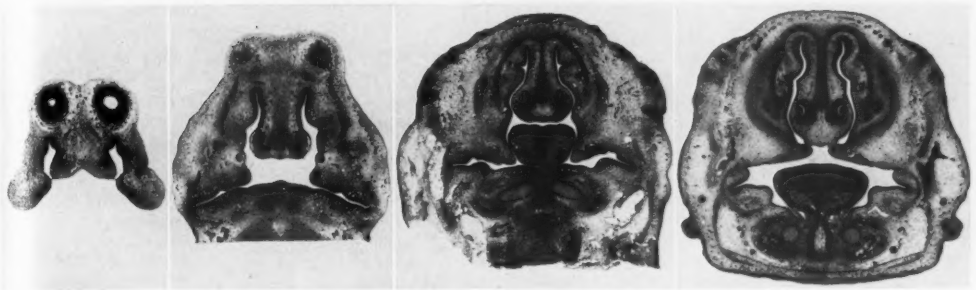

FIG. 4. FIG. 6. FIG. 8. FIG. 10.

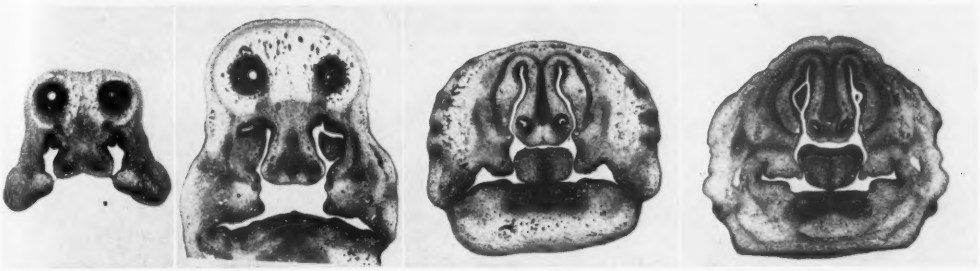

FIG. 5. FIG. 7. FIG. 9. FIG. 11.

FIGS. 4 to 11. Photomicrographs of histologic sections of fetal rat heads (frontal plane) showing morphogenesis of the palate and related structures. Figures 4, 6, 8, and 10 illustrate controls at fetal ages of 13, 14, 15, and 16 days, respectively. Figures 5, 7, 9, and 11 illustrate PGA-deficient fetuses of ages corresponding to the controls. ×11.8.

ternal dietary deficiency. The tongue has remained high in the mouth, close to the nasal septum and retains its trapezoidal shape in cross-section (Fig. 11). The lateral palatine processes are thus trapped below the lateral border of the tongue, in contrast to the normal position (Fig. 10). The PGA-deficient fetus is scarcely larger than on the previous day.

DAY 17. In the normal fetus complete separation of the nasal and oral cavities has been achieved by closure of the nasopalatine canal and by continued junction of the lateral palatine processes in a caudal direction (Fig. 3). This closure obscures from view the definitive choanae or internal nares, by which the nasal cavities communicate with the pharyngeal cavity. Histologic study (Fig. 12) shows that epithelial and mesenchymal fusions are established between the palatine and nasal processes. The epithelium is beginning to assume a stratified squamous form. Intramembranous osteogenesis is in progress in the lateral walls of the nasal cavity but not in the palate.

In the PGA-deficient fetus (Fig. 13) the lateral palatine processes continue to lie below the margin of the tongue. The tongue is appreciably indented where the processes are in contact with it and also shows a depression conforming to the shape of the median nasal process. This fact suggests that growth pressure is being exerted by the lateral palatine processes, not only medially but also dorsally in the direction which these processes should normally have taken. Mesenchymal condensation preparatory for ossification may be seen lateral to the nasal cavity one day later than in controls. The epithelium on the oral surface of the palatine processes has not yet been transformed into the stratified squamous type and the underlying mesenchyme remains embryonic and loose. It frequently showed the first signs of edema which was present in all PGA-deficient young at term.

DAY 18. Normal development at this and subsequent ages is shown only in histologic sections since the gross appearance of the palate achieved by day 17 (Fig. 3) conforms to that at term (Fig. 1a). Palatal rugae are undergoing elaboration as thickenings in the oral epithelium (Fig. 14). The nasal turbinates are becoming more complex. In the deeper tissues, well developed horizontal processes of the maxillary and palatine bone enter the palate. The connective tissues show fibroblasts and collagen fiber formation, and differentiation of skeletal muscle is active.

The PGA-deficient fetus (Fig. 15) shows a persistence of the abnormal topographic relationships of tongue, palatine, and nasal processes. Deformation of the tongue by the palatine and nasal processes is more

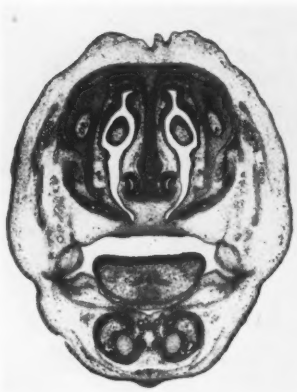

FIG. 12.

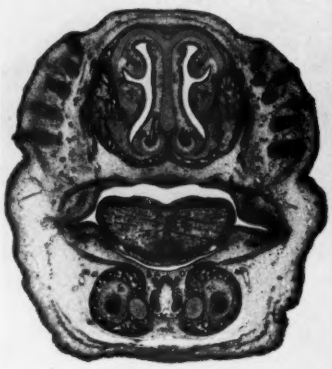

FIG. 14.

FIG. 16.

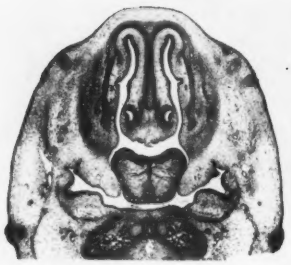

FIG. 13.

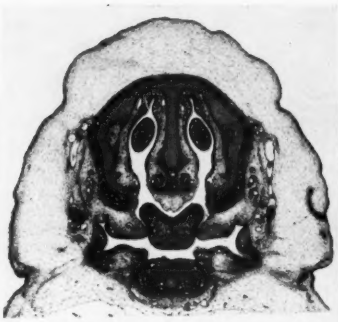

FIG. 15.

FIG. 17.

FIGS. 12 to 17. Photomicrographs continuing the series shown in Figures 4 to 11. Figures 12, 14, and 16 illustrate controls at fetal ages of 17, 18, and 19 days, respectively. Figures 13, 15, and 17 illustrate PGA-deficient fetuses of ages corresponding to the controls. ×10.5.

evident. Edema in the head region has increased. Bone has started to appear in the nasal walls and in the dorsolateral portions of the palatine processes. Although differentiation of the oral epithelium is in progress, connective tissue differentiation is still lagging and little differentiation of skeletal muscle is present.

DAY 19. In the normal fetus (Fig. 16) the principal advance is the bony fusion of the palatine processes in the midline and further differentiation of all tissues.

The PGA-deficient fetus (Fig. 17) shows that the tongue commonly lies lower in the mouth and is no longer clasped by the palatine processes. It may still bear the deformation seen earlier. The processes themselves remain directed ventromedially rather than assuming the normal horizontal direction. Repression of the earlier vigorous growth has left them stunted. Their epithelium and connective tissue show differentiation but little proliferation.

DAYS 20 and 21. The head of the normal fetus (Figs. 18 and 20) shows little change from day 19 except for growth. Roots of the upper incisor teeth are well established in the maxilla lateral to the nasal wall and may be followed back to their first appearance as an epithelial condensation in this region at day 19.

In the PGA-deficient fetus at day 20, no further development of the palate has occurred and the palatal gap persists (Fig. 19). Two illustrations of 21 day PGA-deficient fetuses are shown. Figure 21 presents an animal in which fetal size is almost normal and the edema is only mild. In Figure 22, the two palatine processes differ in their relationship to the tongue, the

FIG. 18.

FIG. 20.

FIG. 19.

FIG. 21.

FIG. 22.

FIGS. 18 to 22. Photomicrographs continuing the series shown in Figures 12 to 17. Figures 18 and 20 illustrate controls at fetal ages of 20 and 21 days, respectively. Figure 19 illustrates a PGA-deficient fetus at 20 days, and Figures 21 and 22 illustrate PGA-deficient fetuses at 21 days. ×7.1.

one on the observer's right occupying a more nearly normal position. The appearance corresponds closely to that illustrated by Walker and Fraser (16) as a fleeting condition sometimes observed in normal mice. In PGA-deficient rats we occasionally have seen one of the lateral palatine processes fused normally with the median nasal process and the other side unfused, resulting in a unilateral palatal defect.

Mandibular development. Micrognathia is a defect encountered in high incidence and in varying severity in fetuses examined at term following PGA deficiency from the eleventh day of gestation. When the deficiency was instituted on the tenth day micrognathia was severe, and occasionally agnathia was observed. Therefore, the development of the lower jaw was examined to determine any possible relationship between its morphogenesis and that of the palate.

In normal development, on day 13 the mouth has not developed to the stage of "closure" (labial contact). It is closed at 14 days, but open again at 15 days, with the tongue protruding from between the lips. Even normally the mandible appears shorter than the nose until day 17. Thereafter, mandibular development begins to accelerate and from the eighteenth day on, the tongue is retracted and the mouth is again closed. Micrognathia is, therefore, difficult to diagnose before the eighteenth day. In addition, the development of edema at this age in PGA-deficient fetuses increases the difficulty of diagnosis from macroscopic inspection. Examination of the intact mandible in alizarin-stained, cleared specimens provided more reliable evidence of retarded and defective mandibular growth.

Normally, the first indications of bone formation in the mandibular body may be seen at 15 days, and extensions of these trabeculae on the sixteenth day indicate the future ramus and coronoid and condyloid processes. A well-formed mandible is present at day 17 (Fig. 23). Its arch broadens rapidly thereafter (Figs. 25 and 27).

In the PGA-deficient fetuses, the mandible is still small and poorly formed on the seventeenth day (Fig. 24). At subsequent ages it remains retarded in size and deformed in shape (Figs. 26 and 28).

It is noteworthy that in normal fetuses Meckel's cartilages could be seen (although not stained by alizarin) only in earlier stages. They were subsequently obscured through investment by intramembranous osteogenesis in the mandibular body. In contrast, in PGA-deficient fetuses Meckel's cartilages were easily visible at the later ages. Often they were abnormal in form, suggesting the shape of a wishbone; the anterior ends of the cartilages came to lie parallel near the midline for some distance. Osteogenesis just lateral to these bars led to narrowing of the arch of the mandible, especially at the level of this midline convergence. Viewed from the lateral aspect, the normal mandible at 21 days is curved with its convexity ventral (Fig. 29). Its length corresponds to that of upper jaw. In PGA-deficient fetus (Fig. 30) the mandible is flat and foreshortened.

The histologic sections also illustrate some of these findings. In normal development midline condensations of mesenchyme are seen in the lower jaw on the fourteenth day (Fig. 6). The jaw is very short at this age, and only its most rostral portion enters the plane of section. On day 15 (Fig. 8) the cartilage bars appear tangential in the section because they are diverging. More laterally mesenchymal condensation indicates the sites where ossification will begin; this intramembranous osteogenesis is active by day 16 (Fig. 10). With further development of the bone Meckel's cartilage becomes fully invested by day 18 (Fig. 14) and more or less completely resorbed by day 20 (Fig. 18).

In PGA-deficient fetuses, individual variation in mandibular development is marked. Mesenchymal condensation preparatory to chondrification is not seen until days 15 and 16 (Figs. 9 and 11), a 1 to 2 day delay in comparison with controls. At the section level used, the cartilage may appear as a single bar (Fig. 15), or be partially divided (Fig. 17), or two bars slightly separated may be found (Fig. 13). Bone formation may occur on the seventeenth day (Fig. 13) or may still be lacking on the eighteenth day (Fig. 15), again a 1 to 2 day delay in comparison with the normal. The mandible was always narrow, and Meckel's cartilage might remain unresorbed even as late as the twenty-first day (Fig. 22).

DISCUSSION

Fraser (2) offers five possible ways in which a cleft palate may develop, namely (a) interference with the build-up of what he calls "shelf force" which tends to bring the palatal processes into their definitive plane, (b) excessive resistance of the tongue, (c) excessive width of the head, (d) narrowness of the palatine processes, and (e) reopening of the closed palate (at present an unencountered and theoretic possibility). He ascribed the cleft palate following maternal cortisone injections in genetically predisposed mouse strains to the first of these mechanisms.

The palatal cleavage demonstrated in the young of rats subjected to PGA-deficiency during the latter half of pregnancy cannot be attributed to a primary defect in the components of the palate, namely the premaxillary and lateral palatine processes. Although fetal growth in general was stunted, there was no evidence for a localized or specific failure of growth in the palatal precursors. On the contrary, there was indirect evidence that the impetus for adequate growth was present and in the right direction. The misshapen tongue suggested pressure from growth of the palatine processes and the processes tended to move into a more horizontal position when the barrier to their di-

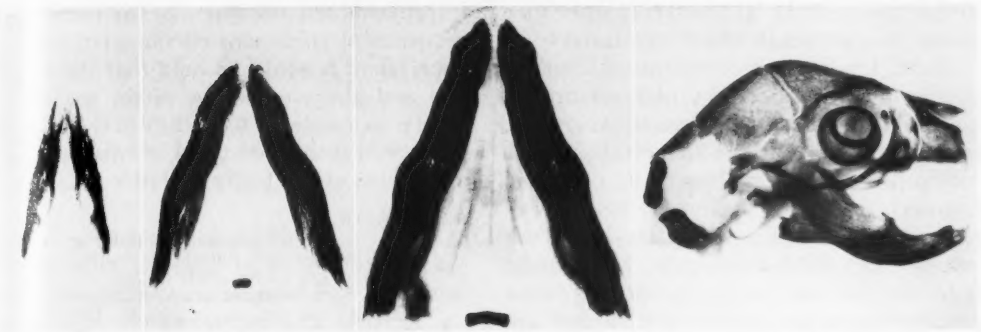

FIG. 23. FIG. 25. FIG. 27. FIG. 29.

FIG. 24. FIG. 26. FIG. 28. FIG. 30.

FIGS. 23 to 28. Ventral aspect of mandible (cleared, alizarin-stained). Figures 23, 25, and 27 illustrate controls at 17, 19, and 21 days fetal age, respectively. Figures 24, 26, and 28 illustrate the effects of PGA-deficiency at ages corresponding to those of controls. The hyoid bone is seen at 19 and 21 days fetal age in both groups. ×5.1.

FIGS. 29 and 30. Lateral view of the cleared, alizarin-stained heads of control (above) and PGA-deficient (below) 21 day old rat fetuses. ×3.15.

rectional growth was removed. The immediate factor in the defect may thus have been the failure of the tongue to descend (Fraser's second mechanism, *vide supra*). The underlying cause was probably a faulty development in the floor of the mouth, particularly the failure of adequate growth and arching of the mandible. Later, when mandibular development reached the stage where the tongue could recede, the local growth impetus in the palatine process had passed, and differentiation, i.e., transformation of the mesenchyme into a fibrous connective tissue and conversion of the epithelium into the stratified squamous type, was predominant. Meanwhile, the breadth of the head had increased, and the lateral palatine processes were unable to meet and fuse.

Evidence supporting this concept of the role of the mandible has been reported by Trasler and associates and by Walker (15). In experiments in which amniotic fluid was withdrawn, the resultant reduction of hydrostatic pressure in the amniotic cavity allowed the uterus to compress the fetus. A high incidence of cleft palate was observed. It was hypothesized that the compression of the fetal head against the thorax resulted in the lower jaw pressing the tongue against nasal septum. The palatine processes were thus denied normal change of position.

Correct ascription of the primary cause is important in determining the time sequence in development of the defect. The lateral palatine processes failed to assume their normal position on the sixteenth day, 5 days after the onset of the maternal dietary deficiency. However, the delay in mandibular

development could be observed earlier, between the fourteenth and fifteenth days.

Patten has listed six developmental mechanisms to be considered in interpretation of congenital defects. Of these, retarded growth or "developmental arrest" is most applicable to the present studies. However, a caution has been offered by Asling (1) against extending this generally to palatal defects resulting from PGA deficiency. The defects described here are simple; a report in preparation shows that more complex and bizarre malformations are encountered when a short term acute PGA deficiency is used earlier in gestation. Their explanation invokes added developmental mechanisms.

SUMMARY

1. The development of cleft palate resulting from maternal deficiency of pteroylglutamic acid during the latter part of gestation has been studied and compared with normal palatal development in rats of the Long-Evans strain. When the deficiency was instituted on the eleventh day of gestation, 95 per cent of the young at term had cleft palates. The incidence rose to 100 per cent when the deficiency was instituted 1 day earlier, but was negligible in deficiencies starting on the twelfth day and thereafter.

2. Studies on the normal development of the palate in rats show that the lateral palatine processes maintained a ventromedial direction under the lateral margins of the tongue until the sixteenth day. Thereafter the tongue lay lower in the mouth and the lateral palatine processes moved into a horizontal position, established contact with the median nasal process, and fused to form the oral roof. In fetuses from PGA-deficient mothers the tongue was high in the mouth until the eighteenth day, with the lateral palatine processes maintaining their position under its margin. Thereafter a palatal gap persisted, though the tongue descended.

3. Micrognathia, in varying degree, was frequently an accompanying deformity. Development of the lower jaw in PGA-deficient fetuses was retarded from the fourteenth or fifteenth day of gestation. In the particular sequence of conditions encountered in this experiment it could be held that the small size and abnormal shape of the mandible were responsible for the failure of the tongue to descend and to permit the normal position and fusion of the lateral palatine processes.

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THE CAUSE AND TREATMENT OF EDEMA OF THE ARM FOLLOWING RADICAL MASTECTOMY

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OUR OBSERVATIONS on edema of the arm developing after radical mastectomy have led us to conclude that thrombophlebitis is the main causative factor and that the lymphatics in the vascular sheaths are also involved. Recognition of this fact has offered the prospect of prophylaxis and treatment by clot solvents and anticoagulants. Thrombophlebitis of the veins of the arm and axilla occurs in a large number of patients immediately after radical mastectomy. Edema of the arm, proportional to the degree and site of vein and lymphatic involvement, develops in a few days or weeks. This is the same clinical picture seen in thrombophlebitis of the lower extremities.

SUGGESTED CAUSES IN THE LITERATURE

As early as 1921, Halsted noted the similarity between scrotal edema after groin resection and edema of the arm after radical mastectomy. His patient was a young man who had recurrent erysipeloid episodes. We have made the same observation in some of our patients who have edema of the arm. Halsted found that radical excision with resection of the axillary vein and a portion of the subclavian vein was not sufficient to produce excessive edema and thought that infection, perhaps unnoticed, was a necessary factor. Homans concurred in this opinion, and Adams reached the same conclusion in experimental work on dogs.

Devenish and Jessop concluded that lymphatic obstruction alone could cause lymphedema and that sepsis, recurrent inflammation, or roentgen ray therapy was not necessary for its development. Nevertheless, they cited 1 case of extensive thrombosis of the main venous channels in which complete lymphatic stasis was present. When the swelling subsided, lymph flow became normal, as shown by dye injection of the lymphatics.

Veal and Hoopes and McGraw believed that edema usually occurred 3 to 6 months after operation, contrary to our experience with closely observed patients in whom it occurred most often within a few days. Veal thought that late scarring and recurrent carcinoma were the causes of edema, again an idea to which we cannot subscribe.

Wound infection and roentgen ray therapy were cited by Daland as the most important factors in the production of edema of the arm after radical mastectomy. Despite his opinion that its occurrence is rare, he reported moderate to severe edema in 21 of 91 cases (23 per cent).

Holman, McSwain, and Beal, reporting on 100 cases of radical mastectomy, presented an interesting survey of conditions that do not cause arm edema. These conditions are listed in Table I, a modification of the table presented by these authors. Holman and his co-workers emphasized two points with which we wholeheartedly agree: (1) unless the arms are measured, significant degrees of swelling may go unrecognized; and (2) the time interval recorded for the appearance of edema postoperatively varies from 2 weeks to 4 months; this recorded date is often later than that of the actual appearance of edema.

A possible traumatic factor in the cause of postoperative edema may be extreme abduction of the arm at operation, the same position thought to produce idiopathic thrombophlebitis of the arm known as "straphanger's disease." Paget called this

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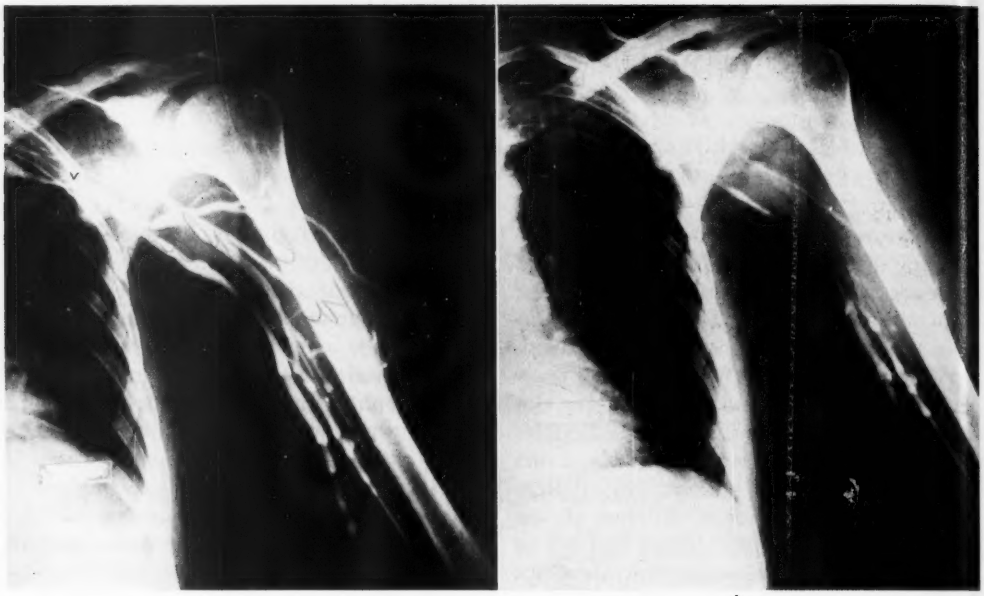

a b

FIG. 1. Pulmonary infarct occurred 7 days after left radical mastectomy and 27 days before roentgen ray treatment, with clinical evidence of phlebitis of the left arm. Venograms 49 days after operation: a, Marked narrowing of axillary, basilic, and brachial veins; note filling of the collateral veins in the shoulder, arm, and chest. b, Delay in clearing brachial and basilic veins, although collaterals have emptied. The arm was still swollen 2 years later.

"gouty phlebitis" in 1875. Kaplan, Clute, Sampson, and Lowenstein attributed idiopathic phlebitis to compression of the subclavian vein between the coracoid process and the first rib.

Lobb and Harkins, reporting on 65 cases of radical mastectomy in which arm measurements were studied, found that a measurable swelling of the ipsilateral arm developed in 80 per cent of patients and that 22 per cent had a measurable difference of at least 3 centimeters. They stated that the correlation between arm edema and the presence of either skin recurrence or impaired arm function was slight, whether or not roentgen ray treatment had been given. MacDonald stated that postmastectomy arm edema was the result of lymphatic obstruction and was not dependent upon venous destruction or resection. He believed that when resection of the axillary vein was necessary, a section of vein was eliminated containing altered lymphatics that ordinarily would set the stage for the occurrence of postoperative edema.

Russo and his associates (16, 17), pioneers in the application of venography to this problem, are convinced that lymphedema and changes of the axillary vein have a close relationship, whereas we believe we are dealing with a thrombophlebitis of one or more main venous channels, with the ever-present lymphangitis in the vascular sheath.

The phlebographic method of studying the swollen arm after radical mastectomy was reviewed by Schorr and his associates in 1954. No correlation was found between the state of the veins in the axillary region as seen in the phlebogram and the presence of swelling of the arm. They stated that many apparent deformities were not necessarily pathologic. Obstruction of the axillary vein

was demonstrated satisfactorily to them only if the narrowing was associated with the presence of collateral veins.

Ever since Halsted developed a technique for radical dissection of the breast and axilla for mammary carcinoma, according to Lipsett and co-workers, postoperative swelling of the ipsilateral arm has been accepted as a common and unavoidable complication in 41 per cent of patients with operable carcinoma of the breast.

Before the days of roentgen ray therapy, lymphedema was attributed to destruction of the bottleneck lymphatic drainage through the axilla. Since the introduction of roentgen ray therapy, the slow fibrotic effect of irradiation has also been accused.

FIG. 2. Infrared photograph showing clinical phlebitis with distended, visible antecubital lymphatics and superficial veins in the upper arm, first observed 18 days after radical mastectomy.

THROMBOPHLEBITIS AS THE ETIOLOGIC FACTOR

Clinical evidence. One patient was observed in 1956 in whom massive lymphedema in the presence of an infected sloughing wound occurred 7 days after radical mastectomy had been performed on the left side and 27 days before roentgen ray therapy was begun. The particular event that incited suspicion of thrombophlebitis as a factor in the cause of the lymphedema was the occurrence of a pulmonary infarct, confirmed by roentgenography. A venogram made 49 days after operation and after 37 days of anticoagulation therapy revealed greatly narrowed brachial and basilic veins (Fig. 1). Although this might be interpreted as fibrotic pressure on these veins at the level of the upper third of the humerus, it must be remembered that pulmonary embolism had occurred without the development of thrombophlebitis in the legs or any previous history of thrombophlebitic disease. Furthermore, the narrowed veins were not at the level of the axilla. Despite 75 days of anticoagulation therapy begun 12 days after operation and 5 days after symptoms had developed, the circumference of the left forearm remained 1 inch greater than that of the right arm 2 years after mastectomy.

Another patient who further aroused our interest was seen 20 months later. This patient was referred to the Lahey Clinic for 2 million electron volt (mev.) roentgen ray therapy after a modified radical mastectomy on the right side had been performed elsewhere. She first noted pain in the medial side of the right upper arm about 1 week after operation and 1 month before roentgen ray therapy was begun. On initial examination, the right arm was cyanotic, a tender vein in the cubital fossa was palpable, tenderness along the course of the brachial vein was elicited, and the lymphatics and superficial veins in the upper arm were visibly distended (Fig. 2). Unfortunately, no venogram was made at that time.

The patient was given penicillin and anticoagulant therapy as an ambulatory patient. Her condition was maintained with good control of prothrombin time for a total of

TABLE I.—CONDITIONS THAT DO NOT CAUSE EDEMA OF THE ARM

Condition	*No. of cases*	*Per cent with edema*
Primary skin graft	71	65
No skin graft	29	83
Positive axillary nodes	32	66
No positive axillary nodes	69	71
Roentgen ray treatment	66	74
No roentgen ray treatment	35	62
Wound infection	44	83
No wound infection	59	54
Skin recurrences	5	60
Per primam healing	14	57
Secondary healing	86	72

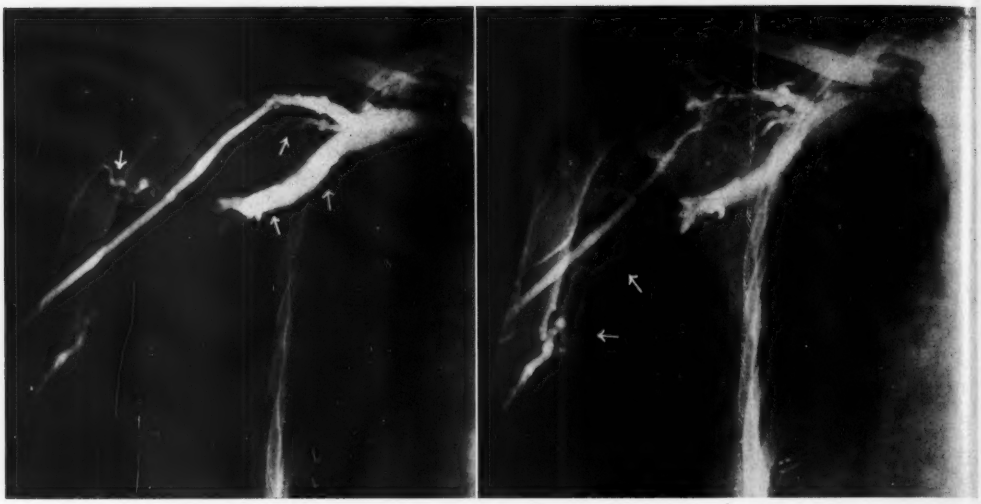

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FIG. 3.

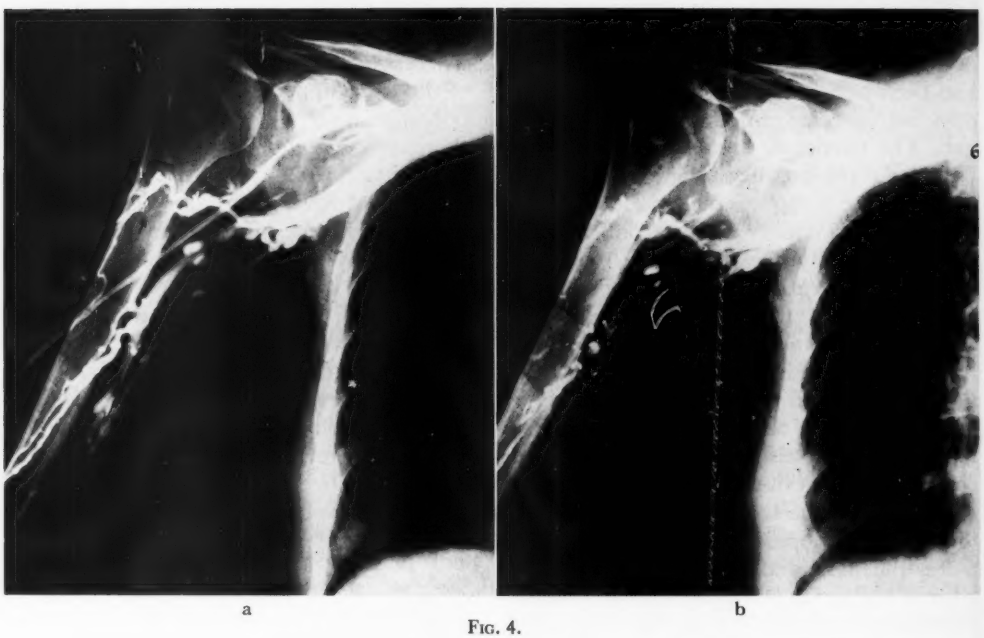

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FIG. 4.

FIG. 3. Symptoms of phlebitis observed 1 day before roentgen ray therapy was started. Venograms: a, Good cephalic, subclavian, and axillary veins fill retrograde; note collateral veins. b, Poor filling of brachial or basilic veins; see "catheter effect" of thrombus.

FIG. 4. Same case as shown in Figure 3, 2 months later. Venograms made after anticoagulation therapy: a, Brachial veins filled and valves preserved. Arrow points to persistent dilated collateral veins. b, Note delay.

70 days. On the seventh day of anticoagulation therapy the swelling had diminished and by the tenth day tenderness had disappeared. At the end of anticoagulation therapy a venogram showed only narrowed brachial and axillary venous channels with no delay in emptying. Eight and one-half months after operation no edema was visible and the patient had a normally useful arm.

Although no venogram was taken to prove that venous obstruction was present when the diagnosis of thrombophlebitis was made and anticoagulation therapy was instituted, the clinical evidence of thrombophlebitis was overwhelming. The prompt, symptomatic response to therapy within 7 to 10 days in a patient who had had symptoms for 1 month was characteristic. Lymphatic obstruction is considered part of the mechanism of the swelling of thrombophlebitis and it was visibly present and was reversible, since no swelling was apparent 9 months after operation.

In a third patient a thrombus that was outlined by venography disappeared after 19 days of anticoagulant therapy. Unfortunately, when therapy was discontinued, relapse occurred (Figs. 3 and 4). The first symptoms of phlebitis had appeared 1 day before roentgen ray therapy was started. Despite a second course of anticoagulant therapy, the arm remains swollen.

Relation of roentgen ray therapy to phlebitis. Because of the evidence that postmastectomy swelling of the arm might be the result of phlebitis, we began at this point referring our roentgen ray therapy patients to the vascular section if suspicious signs of phlebitis were noted.

Of 27 patients sent for 2 mev. therapy in 1958, clinical evidence of phlebitis was found in 23 (85 per cent), and this clinical suspicion was confirmed by venography in 18. All 27 had undergone radical mastectomies performed by 8 members of our surgical staff and 7 surgeons elsewhere. Eighteen patients were treated by anticoagulation therapy—11 by acenocoumarol (sintrom) and 7 by fibrinolysin (actase).

FIG. 5. Infrared photograph showing development of visible collateral veins over arm, shoulder, and chest, indicating thrombophlebitis.

Two patients refused this treatment. The phlebitis was quiescent when recognized in 3 patients and too late for treatment. Only 1 patient had a previous history of phlebitis.

That roentgen ray therapy is not responsible is borne out by the fact that clinical evidence of phlebitis was observed in 12 of these patients as long as 37 days before roentgen ray treatment was started.

In 5 other patients not included in this series, roentgen ray therapy could not have been a factor in the cause of the phlebitis. In 1 of these, phlebitis developed 6 years after mastectomy, and only the mediastinum had been treated by irradiation. In 2 other cases of phlebitis proved by venogram, radical mastectomy was carried out but roentgen ray therapy was not given. Two patients who had a radical mastectomy died of pulmonary embolism a few days after operation.

In our opinion, roentgen ray therapy is not responsible for swollen arms after mastectomy. Supervoltage roentgen ray ther-

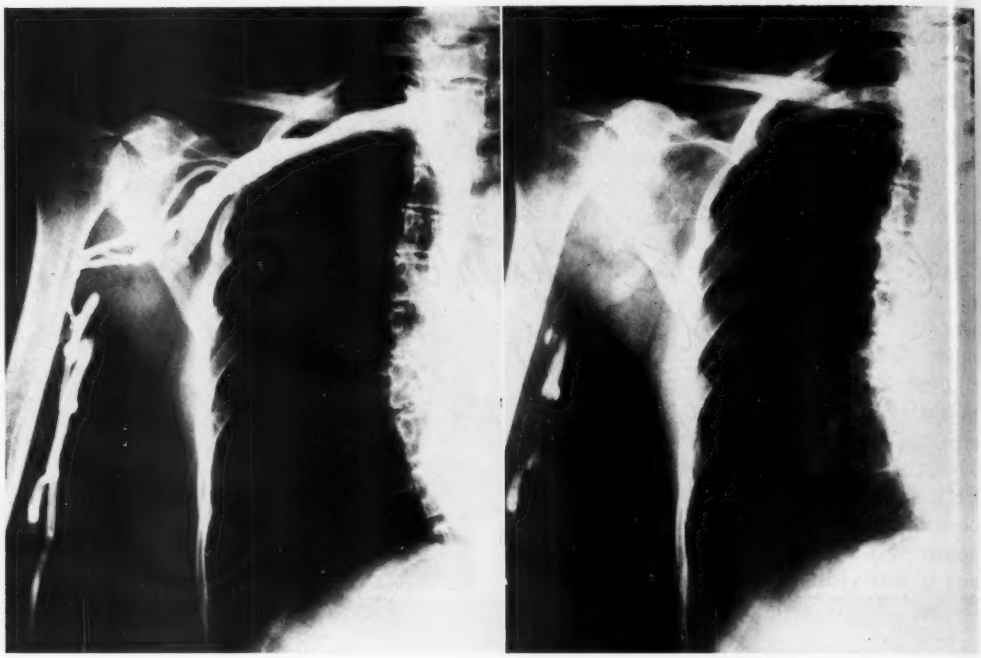

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FIG. 6. Edema and phlebitis 6 years after radical mastectomy and irradiation directed only to the internal mammary area. Venograms: a, Brachial and comitans veins blocked; no basilic vein; note collateral vessels. b, Delayed clearing around valves.

apy, which has sometimes been blamed, cannot be the etiologic factor because, of 16 patients who had radical mastectomy and who received 400,000 volt therapy in 1957, 12 had a swollen arm.

Impressed by the frequency of phlebitis in swollen, painful arms after radical mastectomy, we reinvestigated 28 patients who had received 2 mev. roentgen ray therapy in 1957 after mastectomy. Radical mastectomy was performed in 23 cases, simple mastectomy in 5. Evidence of phlebitis was not recognized during the postoperative period of hospitalization or during roentgen ray therapy. When we reviewed these cases a year later, 18 of the 23 patients who had had radical mastectomy had swollen arms. In 2 patients with a stage 4 carcinoma who had a simple mastectomy and roentgen ray therapy, transient swelling occurred 3 and 14 months after operation. Venography was performed in 7 of these 23 patients who had radical mastectomy and all 7 showed evidence of venous thrombosis.

Relation of radical mastectomy and stage of cancer to phlebitis. In the years 1957 and 1958, simple mastectomy with or without roentgen ray treatment was performed on 23 patients; postoperative swelling of the arm occurred in 3 (13 per cent). In 1 patient the carcinoma was stage 1 and in 2 it was stage 4. McWhirter states that edema is seldom seen after simple mastectomy.

A sloughing wound is not the great factor in causing phlebitis, because among both the patients with suspected phlebitis and the nonsuspected phlebitis controls, slough or massive inflammation occurred in only 2 cases.

Radical mastectomy was performed in 40 additional cases in 1957 and 1958, but roentgen ray treatment was not given and

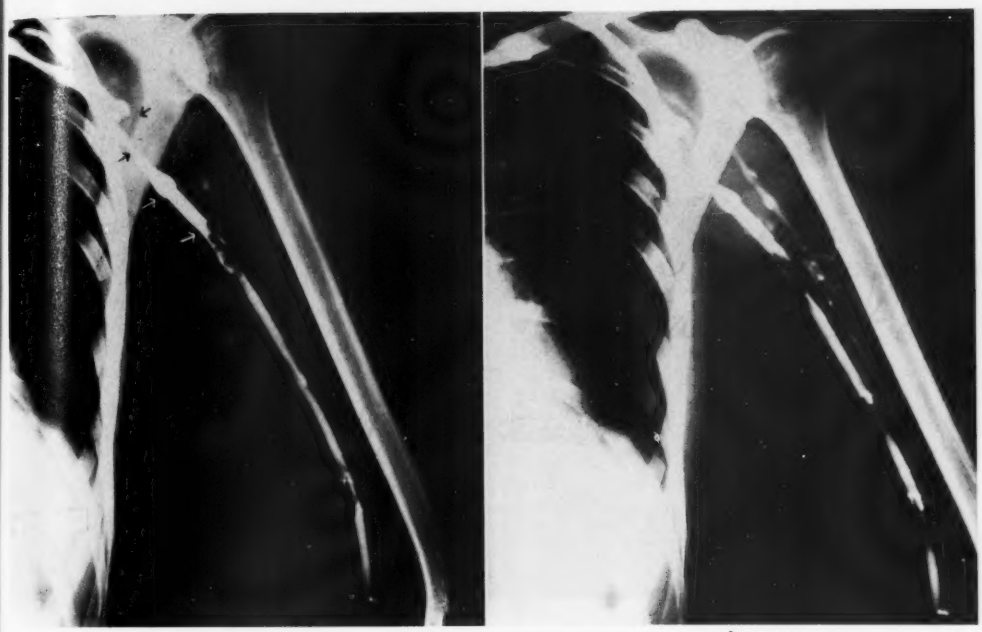

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FIG. 7. Sixteen days after left radical mastectomy, arm was cyanotic and edematous and distended veins were prominent. Venograms: a, Defects in basilic vein (? brachial vein) produced by thrombi at two lower arrows. b, Small collateral vessels immediately bridging defects; arm remains moderately swollen despite anticoagulation.

the patients' courses were followed up by only the surgical department. In 29 patients the lesions were stage 1. Since comments concerning the arm were rarely made in the follow-up observations, presumably the arm was normal. Notes were made in 10 cases, however, that in retrospect raise the suspicion of the possibility of phlebitis. These comments included: "soreness along the axillary nerves," "pain in axilla radiating to elbow," "soreness and swelling of arm," "pronounced edema of the dorsum of the hand," and "cellulitis of the arm." In 2 patients the possibility of phlebitis was recognized—in 1 patient 1 month after operation, and in the second after venipuncture on the operative side 16 months after mastectomy. Previous phlebitis was suspected in this last case because postoperative soreness and swelling had been present but had disappeared months before. Venograms showed positive signs in these 2 cases.

The relative infrequency of proved phlebitis in this control group of 40 patients subjected to radical mastectomy without roentgen ray therapy—a suspected 30 per cent as opposed to 85 per cent proved in the roentgen ray treated group—can be accounted for by two facts: first, the observers were not looking for phlebitis, and second, the group given irradiation was heavily weighted with a more advanced stage of carcinoma. In the nonirradiated group, stage 2 and 3 lesions were present in only 27.5 per cent, whereas in the group chosen for irradiation therapy 85 per cent of the lesions were in stages 2, 3, and 4, indicating that carcinoma was present in the axilla, outside the breast, or both (Table II).

Alertness and increasing evidence. Interestingly, by 1958 when we were looking for swollen arms in patients who had had radical mastectomies, swelling was found in 23 (85 per cent) of the 27 patients sent to the radi-

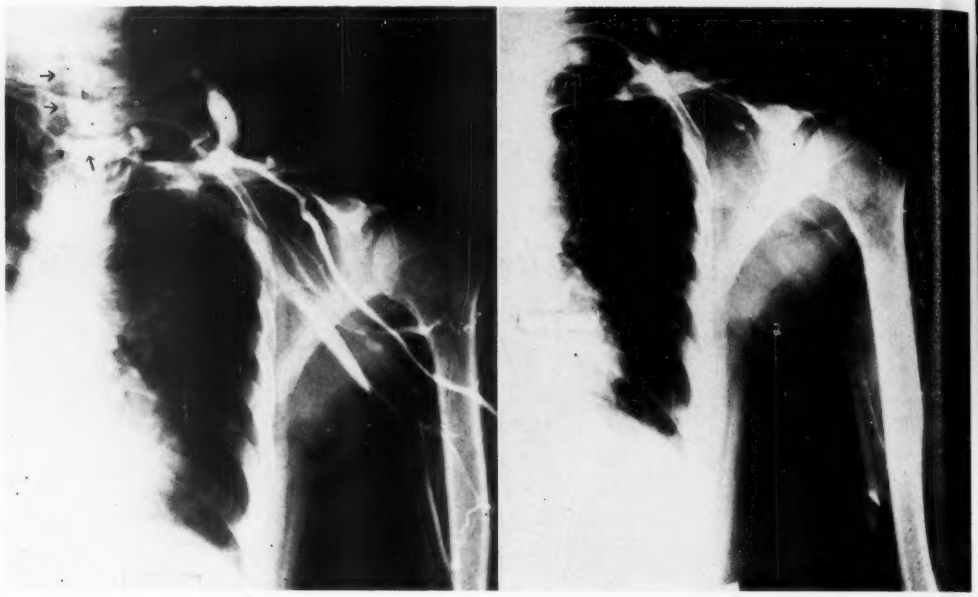

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FIG. 8. Thirty-five days after left radical mastectomy and on the twenty-fourth day of roentgen ray treatment, this patient complained of pain in the arm; the brachial area was swollen and tender. The patient was hospitalized and given anticoagulants for 12 days. The arm has remained swollen (arm, grade 1, forearm, grade 2). Venograms 5 years after operation: a, Axillary vein blocked; pronounced filling of collateral veins; note jugular arch and retrograde filling of jugular and vertebral veins. b, Delay in emptying.

ology department for therapy. In 1957 and 1958 venography was performed on 27 patients with swollen arms; positive evidence of phlebitis was found in 25. This was manifested by one or more of the following factors: obstruction, outlining of a thrombus, delay in emptying, and development of collateral vessels. In the remaining 2 cases, the venogram was technically unsatisfactory in one, and the dye passed rapidly through the veins in the other.

TABLE II.—ROLE OF STAGE OF LESION

	No.	*Per cent*
Without roentgen ray therapy	40	
Swollen arm		10.0
2 mev. therapy	60*	
Swollen arm		85.4
Nonirradiated group	40	
Stages 1 and 2		27.5
Irradiated group	60*	
Stages 2, 3, and 4		85.0

*27 patients in 1957; 28 patients in 1958; 5 patients who did not have mastectomy.

Favorable conditions for the development of phlebitis. Five conditions favor the development of phlebitis: previous history of phlebitis, inanition, immobility of a limb, extensive surgery in the vicinity of large venous trunks, and cancer. The first two factors were not present in this series. In our department of surgery, great care has been taken to mobilize the arm immediately, but in 6 patients bursitis was definitely mentioned as a complication and 5 of these had swollen arms. In 2 of the 6 patients with bursitis, the venograms demonstrated the presence of an obstruction or outlined a thrombus.

The fact that metastatic lymph nodes were present in the axilla in 25 of 27 patients with positive venograms emphasizes the role of cancer as a predisposing factor for the development of thrombophlebitis. To classify these 27 cases into stages of cancer based on Portmann's classification, 2 were

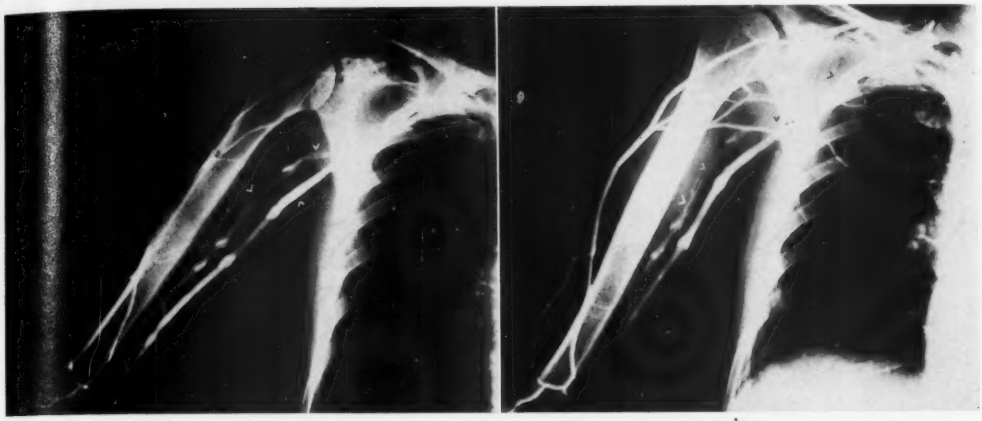

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FIG. 9. Ten days after right radical mastectomy, pain occurred in arm, antecubital fossa, and axilla; edema was present with distention of the veins of the shoulder. Venograms: a, Brachial thrombus with "catheter effect"; obstruction of axillary and cephalic veins; note collateral vessels in shoulder. b, After actase; tenderness disappeared in 5 days; no entrance of contrast medium into cubital vessels. Note persistence of obstruction and pronounced filling of collateral veins over chest wall.

stage 1 (no cancerous lymph nodes), 16 were stage 2 (less than half of the axillary lymph nodes were cancerous), 8 were stage 3 (massive axillary involvement), and 1 was stage 4 (massive involvement of axilla and skin). Since a swollen arm developed in only 13 per cent of patients with a simple mastectomy, we must conclude that extensive surgical procedures near the axillary vein and the presence of carcinoma in the axilla are the two predominant causative factors.

DISCUSSION

The proof of our thesis that arm edema after radical mastectomy is the result of thrombophlebitis is at present based primarily on a clinical appraisal. The clinical evidence outweighs the evidence by phlebography because many weaknesses apparently exist in the art of phlebography at the present time. Cinetechnique before and after operation would undoubtedly add to the accuracy of the observations.

No actual statement that one is dealing with thrombophlebitis has appeared in publications on postmastectomy swelling of the arm. We believe this problem is no different from that which the obstetrician or pelvic surgeon faces in postoperative phlegmasia alba dolens. The anatomic parallel between the sites of the iliofemoral thrombophlebitis and the brachial axillary subclavian veins of the upper extremity is obvious. We believe the pathologic process is the same "sheathitis" of a major vascular trunk, as Homans noted in 1937 in describing the femoral vascular trunk syndrome. One is dealing with an inflammatory obstruction of the lymphatics in the perivascular sheath, with thrombosis in a major vein, and sometimes arterial spasm. Furthermore, in support of the fact that thrombophlebitis is the etiologic factor in the production of edema of the arm after radical mastectomy, we add to the 2 cases previously reported in the literature 2 cases in which death resulted from pulmonary embolism.

Several factors increase the probability of the occurrence of thrombophlebitis: (1) abduction of the arm during operation, as in "straphanger's" phlebitis of the arm; (2) impairment of venous return, which could be caused by pressure from a bandage, a tight binder, or the position of the extremity, with

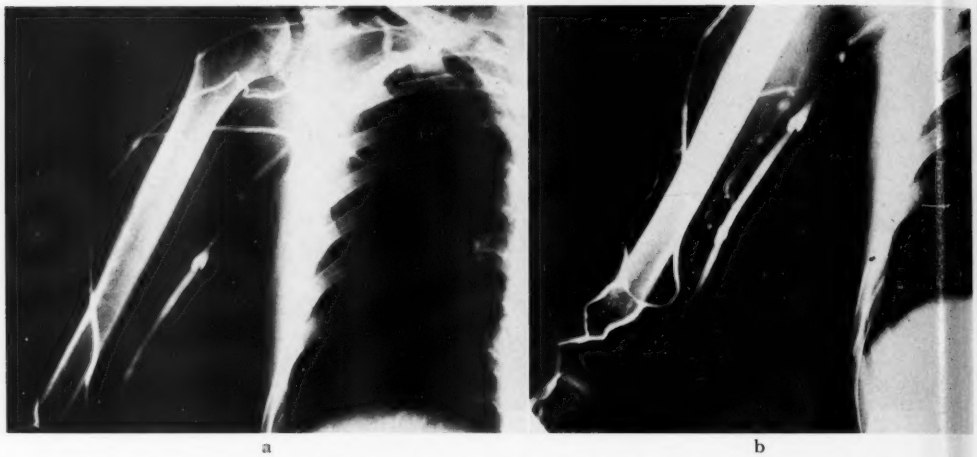

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FIG. 10. Same case as shown in Figure 9, 3 months after operation. The arm is still swollen. Venograms: a, Well-developed collateral circulation over shoulder. b, Halfway through injection, note retrograde filling from needle point and filling of brachial vein from collateral vessels above and below elbow level.

resultant slowing of the venous return—if this happened at a point where there are cross currents from many tributaries, slowing of the current would favor thrombus formation; (3) trauma to the vein in dissecting the axilla; (4) ligation of large venous tributaries in some cases, although in many of our cases venography has shown thrombosis in the brachial or other major veins of the arm to be well below the site of the subscapular vein; (5) the presence of cancer in the axilla; (6) infection, not necessarily a sloughing wound, but minor, since experimental ligation of the main vascular channels, venous, arterial, or both, fails to produce edema in a limb unless infection is introduced.

The typical clinical signs of thrombophlebitis are identical with those associated with postoperative phlebitis in the leg:

1. Soreness reported by the patient within a few days after operation. The pain may be in the axilla, which is the operative site, and therefore discounted by the surgeon; however, it is also found along the brachial vein in the upper arm, sometimes as low as the cubital fossa, where operative trauma would not produce pain.

2. Tenderness elicited along the axillary and brachial veins and often in a palpable vein in the upper arm or cubital fossa.

3. Swelling of the upper arm, which may escape the notice of the physician if he does not actually measure the arm.

4. Cyanosis of the arm, sometimes paleness.

5. Development of visible collateral veins over arm, shoulder, and chest (Fig. 5).

6. Visible distention of subcutaneous lymphatics in the arm or antecubital fossa (Fig. 2).

7. Pain on stretching the involved vein by extending the elbow—the same principle as in Homans' sign.

8. Finally, although rare in phlebitis of the arm as in phlegmasia alba dolens, pulmonary embolism from the involved arm, as we have seen twice. In 1 of these cases, embolism was proved at autopsy and in the other by typical symptoms and evidence in the chest roentgenogram.

Venography offers direct evidence proving the presence of venous thrombosis. Five abnormalities shown in the venogram confirm the clinical diagnosis of thrombophlebitis: obstruction (Fig. 6), a filling defect in

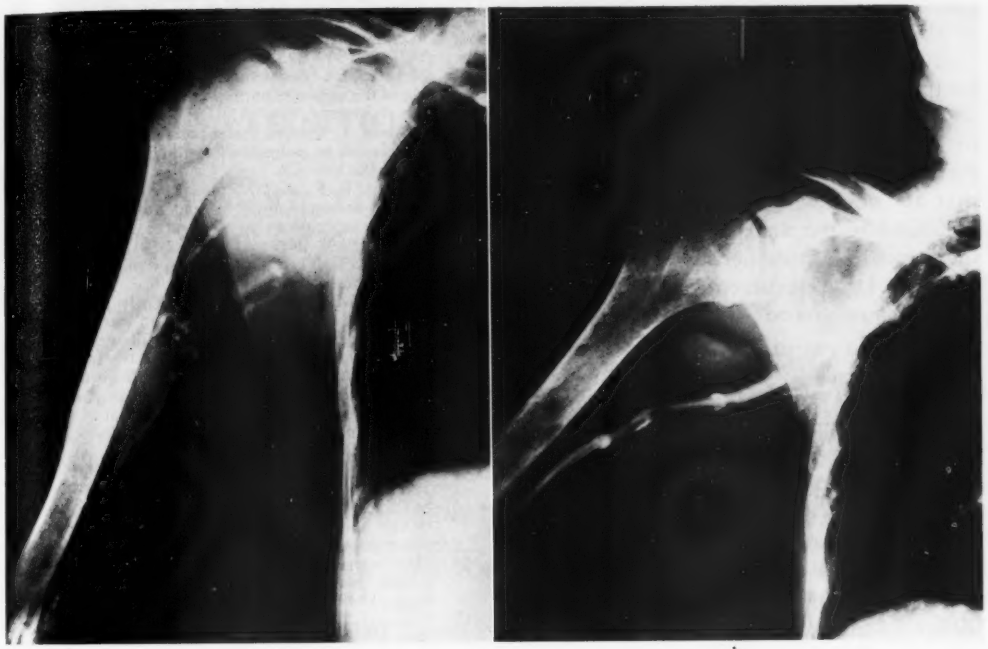

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FIG. 11. Phlebitis occurring 18 years after operation. Venograms: a, Obstruction low in brachial vein; note collateral vessels. b, Thirteen days later, good caliber after administration of fibrinolysin (actase); all clinical signs were absent.

the lumen of a vein not obviously an artifact (Fig. 7), filling of collateral veins (Figs. 8, 9, 10), retrograde filling of veins (Fig. 10), and delay in emptying (Fig. 8).

We do not believe a swollen arm occurring years after mastectomy is necessarily caused by recurrence of the malignant tumor. We have seen it occur as phlebitis, proved by venogram 18 years after operation, with subsequent clearance of the venous channel and rapid disappearance of all the typical clinical signs and symptoms following fibrinolysin therapy (Fig. 11). In another patient a swollen arm occurred 19 months after operation as a result of venipuncture on the ipsilateral arm. Typical recurrent flare-ups of phlebitis occur in some cases, as in chronic recurrent thrombophlebitis of the leg. In such cases, episodes of increased soreness are noted along the course of the brachial vein, accompanied by fever and chills, with erysipeloid reaction of the arm and increased edema.

The plea of Homans regarding postmortem examination of the veins of the lower extremity should be extended to include Halsted's elephantiasis chirurgica of the upper extremity. This means that pathologists should examine the veins of the upper limb in patients who have had swollen arms after mastectomy.

Recognition of the swollen arm syndrome as thrombophlebitis after radical mastectomy is important for its prevention and treatment. There are now anticoagulants for prophylaxis, and clot solvents for possible cure if the condition is recognized early.

CONCLUSIONS

Edema of the arm after radical mastectomy is caused by thrombophlebitis with

concomitant obstruction of the lymphatics in the vascular sheath. The condition is analogous to the familiar postoperative or postpartum phlegmasia alba dolens of the leg. The importance of its recognition lies in the possibility of prophylaxis and treatment by anticoagulants and clot solvents that are now available.

Edema of the arm is most often seen in the immediate postoperative period. When it occurs later, recurrent thrombophlebitis is the cause more often than recurrent cancer.

A swollen arm was found in 57.5 per cent of all patients seen at the Lahey Clinic who had radical mastectomy in 1958. Of the patients referred for roentgen ray therapy after radical mastectomy, 85 per cent had postoperative swelling of the arm; 45 per cent of this group had swelling of the arm before roentgen ray treatment was started.

Five abnormalities in the venogram confirm the clinical diagnosis of thrombophlebitis: (1) obstruction; (2) a filling defect in the lumen of a vein, not obviously an artifact; (3) filling of collateral veins; (4) retrograde filling of veins, and (5) slow emptying.

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A PYELOGRAPHIC STUDY OF URETERIC INJURIES SUSTAINED DURING HYSTERECTOMY FOR BENIGN CONDITIONS

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THE PELVIC PORTION of the ureter is vulnerable to injury during gynecologic surgery because it lies in close relation to the uterine artery, the cervix, and the lateral portion of the vagina. Wide variation in the course of the ureter increases the difficulties of surgical procedures, and alterations in position due to pelvic inflammatory disease, tumors, or anomalies of the urinary tract all tend to increase the surgical hazards.

During operation the ureter may be injured by cutting, crushing, ligation, or kinking. These injuries are usually manifested early but may be delayed, particularly if the damage is secondary to interference with the nervous or vascular supply to the ureterovesical area. Complete obstruction of a ureter may be followed by asymptomatic atrophy of the kidney while, if the ureter is severed, a fistulous opening into the peritoneum or the vagina may be the result. An immediate or delayed fulminating renal infection may follow complete or incomplete obstruction. Partial obstruction of the ureter due to compression or marked angulation may cause a progressive hydronephrosis with complete absence of signs and symptoms. The only finding after operation may be a slight elevation of the patient's temperature as well as minimal costovertebral tenderness which can easily be overlooked.

The exact incidence of surgical trauma to the ureter is unknown. It has been estimated by Pfeffer that in radical procedures for gynecologic carcinoma, injury to the ureter occurs in 8 to 30 per cent of cases.

The incidence of ureteral damage following gynecologic surgery for benign disease has been estimated in 12 series of cases since 1902 (Table I). Nine of these series were incomplete since routine preoperative and postoperative urographic examinations were not performed. As a result, only those cases with clinically manifested ureteral disease or those detected at postmortem examination were included while those patients with silent lesions were not considered. In addition, some cases of ureteral disease discovered postoperatively might have been incorrectly attributed to the surgical procedure as there were no preoperative roentgenograms. It is of interest that Newell reported a total of 14 ureteral injuries in 3,144 hysterectomies. Six of these were detected only at necropsy. In the study by St. Martin, Trichel, Campbell, and Locke, 332 patients scheduled for major gynecologic surgery, exclusive of radical surgery, had preoperative excretory urograms. Between the sixth and eighteenth postoperative days all patients underwent ureteral catheterization to determine the patency and functional status of the ureters. The total number of injuries cannot be accurately assessed since excretory or retrograde urograms were only performed in questionable cases. However, they found 8 injuries, an incidence of 2.4 per cent. Five of the 8 patients were considered to have had minor trauma to the lower ureter which resulted in temporary hydronephrosis with spontaneous regression

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TABLE I.—INCIDENCE OF URETERAL DAMAGE AFTER GYNECOLOGIC SURGERY FOR BENIGN DISEASE

Author	*Year*	*Type of operations*	*No. of operations*	*No. of ureteral injuries*	*Percentage of ureteral injuries*
Sampson	1902	Hysteromyomectomies and hysterosalpingectomies	792	7	0.88
Eddy and Miller	1937	Abdominal and vaginal hysterectomy	200	1	0.50
Newell	1939	Abdominal and vaginal hysterectomy	3,144	14	0.45
Wallingford	1941	Total hysterectomies	100	2	2.00
Wallingford	1941	Total and supracervical hysterectomies	4,010	5	0.12
Herman, Greene, and Hayllar	1946	Unspecified gynecologic operations	7,966	4	0.05
Halloway	1950	Abdominal and vaginal hysterectomy	1,620	8	0.49
St. Martin, Trichel, Campbell, and Locke	1953	Major gynecologic surgery exclusive of radical surgery for cervical carcinoma	332	8	2.41
Falk and Bunkin	1954	Major gynecologic surgery for benign disease	6,309	5	0.08
Conger, Beecham, and Horrax	1954	Major gynecologic surgery including radical surgery for cervical carcinoma	2,290	13	0.57
Horrax and Conger	1954	Major gynecologic surgery including radical surgery for cervical carcinoma	200	1	0.50
Benson and Hinman	1955	Major obstetric and gynecologic surgery including cesarean sections and Wertheim panhysterectomies	6,211	30	0.48

by the fifth postoperative week. Three patients had complete unilateral ligation of the ureter. Of these, 2 were completely asymptomatic and the diagnosis was made during the routine postoperative study. In 36 cases (10.8 per cent), hydronephrosis and hydroureter existed prior to operation, but these conditions spontaneously resolved after operation in all but 3 cases. Horrax and Conger carried out preoperative and postoperative excretory urograms on 200 patients who had undergone major gynecologic surgery. They found hydronephrosis before operation in 12 per cent of the patients which was reversed spontaneously in all cases after operation. One patient had a silent postoperative ureteral obstruction, an incidence of 0.5 per cent. In 100 cases reported by Wallingford postoperative excretory urograms revealed 2 unsuspected instances of hydronephrosis and hydroureter. Seven of his patients had anatomic anomalies of the urinary tract.

It is clear from the foregoing data that some ureteral injuries may remain undetected unless routine studies by either excretory or retrograde urography are performed in the postoperative gynecologic patient. Preoperative evaluation should also be done because of the high percentage of patients who show urinary tract abnormalities.

In this study preoperative and post-operative excretory urography was performed in order to determine the incidence of ureteral damage which resulted from the performance of hysterectomy for benign conditions.

MATERIAL

The study was carried out between 10 June 1957 and 9 June 1958. Intravenous pyelograms were performed before and after operation on 200 patients scheduled for hysterectomy. All operations were performed by members of the attending or resident staff and the following types of hysterectomy were performed: total abdominal hysterectomy in 171 cases; vaginal hysterectomy and vaginal plastic, 19; subtotal abdominal hysterectomy, 8; subtotal abdominal hysterectomy and vaginal plastic, 1; and total abdominal hysterectomy and vaginal plastic, 1.

PROCEDURE

It was realized that in order to obtain the full co-operation of the referring physician and his patients it would be necessary, in many instances, to perform the urographic examinations on the day of admission and the day of discharge. As a result, many examinations were conducted without prior preparation of the patient so that roentgenographic detail was sometimes sacrificed for expediency. Despite this handicap, hypaque, the contrast medium used, was secreted in sufficient quantity and concentration for accurate delineation of the entire urinary tract in almost every case.

CASE HISTORIES

CASE 1. This patient was a 48 year old, gravida 2, para 2, who was admitted to Maimonides Hospital on 17 July 1957, with a 2 months' history of excessive menstrual bleeding, increased duration of menstruation, and postcoital bleeding. On examination, the uterus was the size of a 12 weeks' gestation due to a 3 inch subserous myoma in the fundus. The tubes and ovaries appeared normal.

Total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed without difficulty on 18 July 1957. The highest daily temperature ranged from 100 to 100.8 degrees during the first 8 postoperative days. The patient then became afebrile and was discharged on the tenth postoperative day.

The preoperative pyelogram (Fig. 3) was normal except for a large pelvic mass. Pyelography (Fig. 4) 7 days after operation revealed a normal right urinary tract but no function on the left side was seen 25 minutes after injection of the dye.

The patient was readmitted on 5 August 1957. She had had no symptoms or signs referable to the urinary tract and the concentration of the blood urea nitrogen was 11 milligrams per 100 cubic centimeters. An intravenous pyelogram (Fig. 5) revealed faint visualization of a hydronephrotic left kidney after 5 minutes, with better delineation after 15 minutes. The left ureter was uniformly dilated from the ureteropelvic junction to the region of the ischial spine. At this level, it curved sharply toward the midline and was lost in the sacral shadow. The distal end of the ureter was never visualized.

The patient was discharged with recommendation that additional pyelograms should be taken at a later date as there appeared to be an incomplete obstruction of the ureter and only partial impairment of kidney function. Subsequently at another hospital, the ureter was freed with complete reversal of the renal and ureteral abnormalities.

FIG. 1. FIG. 2.

FIG. 1. The preoperative pyelogram shows a large soft tissue mass producing hydronephrosis and hydroureter.

FIG. 2. Seven days postoperatively the dilatation of the urinary tract is completely relieved.

CASE 2. This patient was a 45 year old, gravida 3, para 0, who was admitted because of weakness, weight loss, and an irregularly enlarged uterus. On 15 October 1957, total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. A pedunculated leiomyoma, 5 centimeters in diameter, was attached to the anterior surface of the uterus, and an intramural leiomyoma, 10 to 12 centimeters in diameter, was present in the fundus extending to within 2 centimeters of the cervix. Adhesions in the cul-de-sac between the uterus, peritoneum, and bowel were divided. Several suture ligatures were required to control bleeding on the posterior part of the right broad ligament.

On the third postoperative day bleeding from the lower angle of the abdominal wound was controlled with a pressure dressing. On the sixth postoperative day a small amount of pus was expressed from the wound. The temperature rose to 101 degrees on the first postoperative day, to 101.2 degrees on the second, and to 100.8 degrees on the third. The patient was subsequently afebrile and was discharged.

The preoperative pyelogram (Fig. 6) showed a normal kidney and ureter, but a large pelvic mass caused a deep imprint on the dome of the urinary bladder. The intravenous pyelogram, 6 days after operation (Fig. 7), revealed right hydronephrosis and hydroureter due to an obstruction 5 centimeters

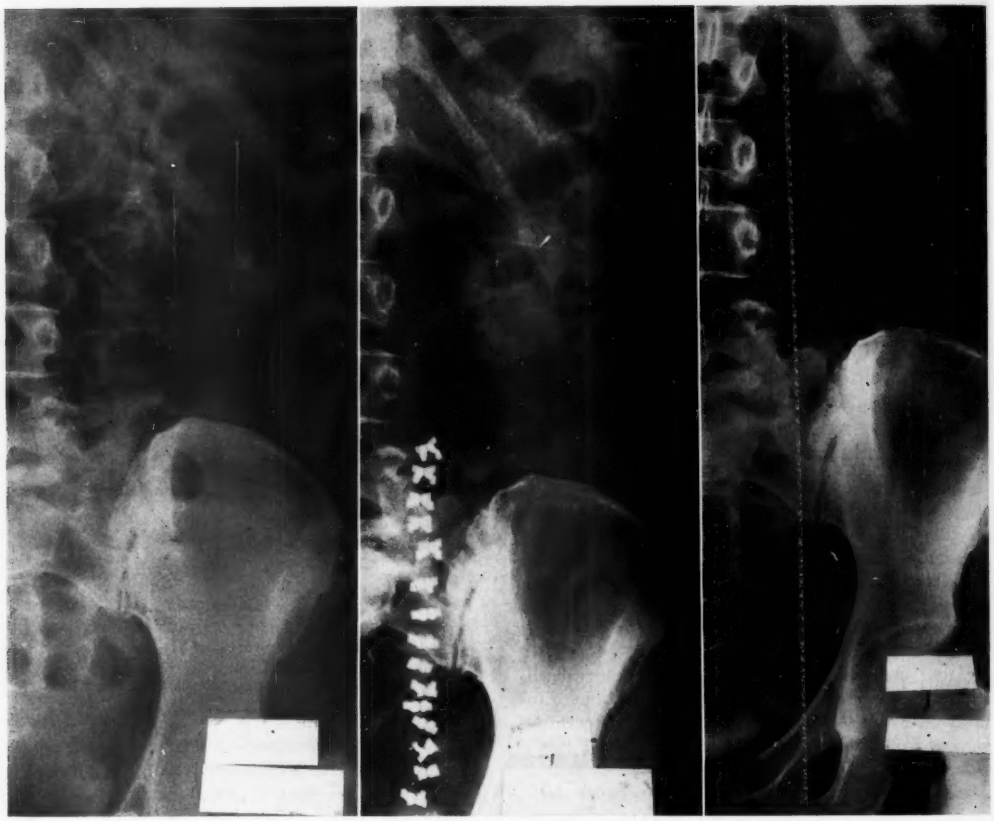

FIG. 3. FIG. 4. FIG. 5.

FIG. 3. Case 1. Normal preoperative pyelogram with poor delineation of the lower end of the ureter.

FIG. 4. Case 1. Postoperatively, there is nonfunctioning of the left kidney.

FIG. 5. Case 1. Twelve days later, there is left hydronephrosis and hydroureter. The lower end of the visualized ureter is deviated medially and the terminal 5 centimeters are not visualized.

proximal to the right ureterovesical junction. There was a sharp "cut-off" at this point but enough contrast material leaked through to demonstrate the distal ureteral segment. Cystoscopic examination 3 weeks later revealed prompt bilateral excretion of indigo carmine, but a catheter could not be passed into the right ureter farther than 4 to 5 centimeters from the entrance of the ureter into the bladder. Subsequent pyelograms revealed a decrease in the amount of dilatation of the renal pelvis and calyces with return to normal 1 year later (Fig. 8).

The concentration of blood urea nitrogen was 13 milligrams per 100 cubic centimeters before operation and 10 milligrams 4 weeks after operation. The patient did not have urinary symptoms at any time after operation.

CASE 3. This patient was a 49 year old, gravida 2, para 0, who was admitted to Maimonides Hospital on 16 December 1957, with a 2 months' history of excessive menstrual and intermenstrual bleeding. Examination revealed the uterus to be irregularly enlarged.

Total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed on the following day. The uterus measured 9 by 6.5 by 4 centimeters. A subserous nodular mass measuring 6 centimeters in diameter was attached to the posterior aspect of the fundus. Several other smaller subserous masses were present. Half of the left ovary was replaced by a thick walled, translucent cyst which was filled with clear, gelatinous material. Microscopic examination of the cyst revealed it to be a papillary serous cystadenocarcinoma.

FIG. 6.

FIG. 7.

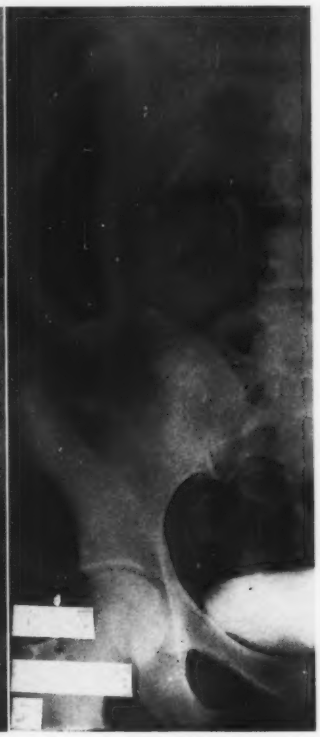

FIG. 8.

FIG. 6. Case 2. A pelvic mass produces a deep imprint on the urinary bladder.

FIG. 7. Case 2. Six days postoperatively, there is right hydronephrosis and hydroureter with a sharp "cut-off" 5 centimeters above the bladder. A small segment of the terminal end of the ureter is visible.

FIG. 8. Case 2. One year later the pyelogram is normal.

FIG. 9. Case 3. Normal pyelogram preoperatively. Note the smooth curve of the lower ureter.

FIG. 10. Case 3. Six days subsequent to hysterectomy, there is minimal left hydronephrosis and hydroureter. Note the sharp kink which is demonstrated at the level of the ischial spine, as well as complete filling of the entire ureter.

The preoperative pyelogram (Fig. 10), on the sixth postoperative day, showed a localized medial kinking of the left ureter just above the level of the ischial spine with hydronephrosis and hydroureter. Unfortunately, this patient was lost to follow-up study.

CASE 4. This patient was a 67 year old, gravida 7, para 7, who was admitted with complete prolapse of the uterus, cystocele, rectocele, and vaginal enterocele. The uterus was normal in size and the tubes and ovaries were not felt. The operation was postponed because the patient had a low grade pyrexia. Subse-

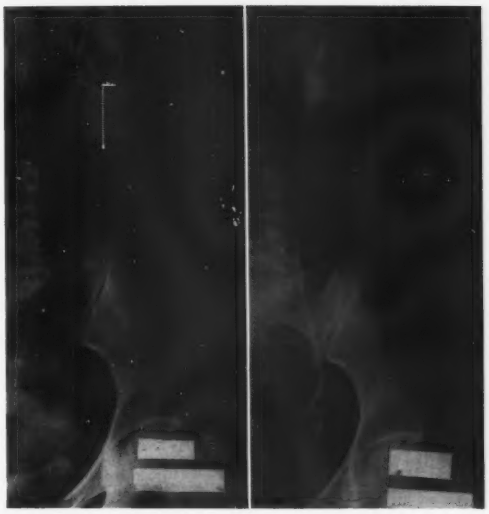

FIG. 9.

FIG. 10.

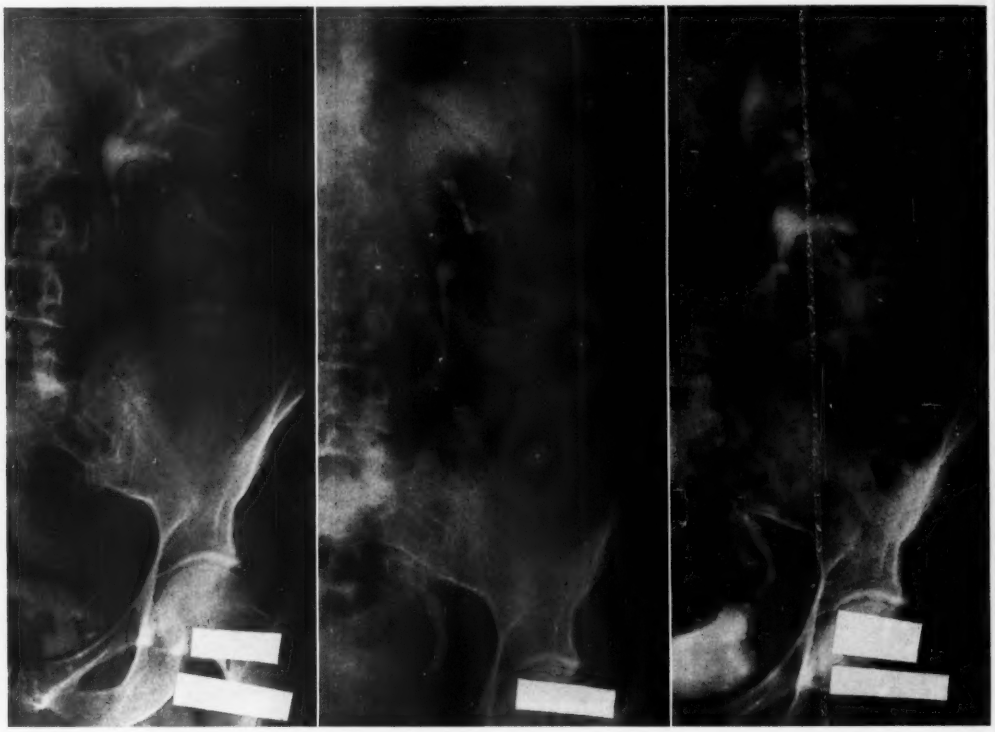

FIG. 11. FIG. 12. FIG. 13.

FIG. 11. Case 4. The preoperative pyelogram is normal.

FIG. 12. Case 4. Six days after vaginal hysterectomy there is dilatation of a short segment of the lower end of the left ureter.

FIG. 13. Case 4. Nine months later, there is now hydronephrosis and hydroureter.

quently, vaginal hysterectomy, anterior colporrhaphy, posterior colpoperineorrhaphy, and repair of vaginal enterocele were performed without incident on 25 February 1958. The temperature rose to 103 degrees on the first and second postoperative days and returned to normal by the fifth day, but recovery was otherwise uneventful.

The preoperative pyelogram (Fig. 11) was normal, but the postoperative pyelogram (Fig. 12) revealed a localized dilatation of the distal 6 centimeters of the left ureter. Nine months later another urogram (Fig. 13) demonstrated hydronephrosis and hydroureter. Follow-up examination on 6 July 1959 showed complete disappearance of the hydronephrosis and hydroureter.

CASE 5. A 49 year old, gravida 5, para 4, was admitted to the hospital on 25 May 1958, with a cystocele, rectocele, and first degree uterine prolapse. Her last menstruation had occurred 5 years previously, but she had had 1 day of vaginal bleeding 3 months prior to the time of her admission. The uterus was found to be normal in size, and the tubes and ovaries were not palpable.

Vaginal hysterectomy, anterior colporrhaphy, posterior colpoperineorrhaphy, and repair of vaginal enterocele were performed. A low grade temperature elevation not exceeding 101.4 degrees was present for 6 days after operation.

On the preoperative pyelogram (Fig. 14), a duplex right kidney pelvis and double ureter were seen but only one of the right ureters was demonstrated in its entire course. After hysterectomy, the upper right renal complex was not demonstrated (Fig. 15), and there was minimal dilatation of the lower right urinary complexes. Five months later a pyelogram (Fig. 16) showed hydronephrosis of the upper right renal complex and its ureter while the lower renal pelvis and its ureter were normal. Since the hydronephrosis of the upper renal complex was minimal, the patient was kept under observation.

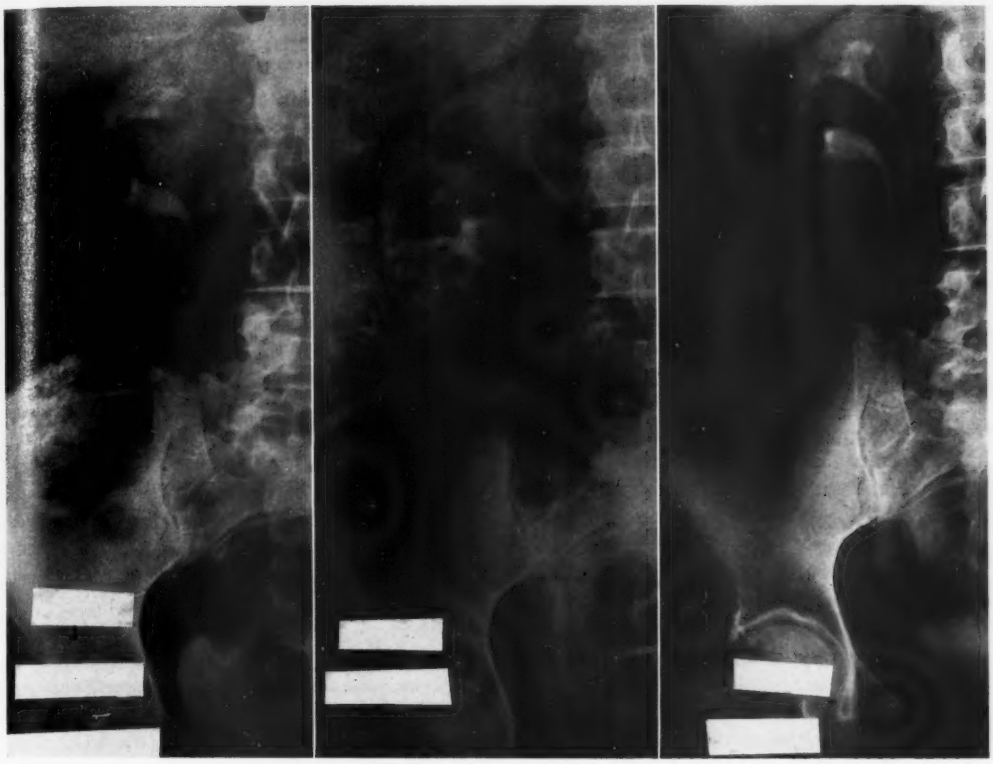

FIG. 14. FIG. 15. FIG. 16.

FIG. 14. Case 5. A duplex right kidney is visible, but the distribution of the ureters cannot be determined.

FIG. 15. Case 5. Seven days postoperatively, there is nonvisualization of the upper complex and dilatation of the lower renal complexes as well as a ureter.

FIG. 16. Case 5. Five months later, the lower renal complexes are normal but there is dilatation of the upper renal complex and its entire ureter.

DISCUSSION

Intravenous pyelography was carried out before and after operation in 200 consecutive patients who had hysterectomy performed for benign uterine conditions, and in 151 patients the pyelograms were normal. In 41 patients there were varying degrees of hydronephrosis, 37 of which reverted to normal after hysterectomy (Figs. 1 and 2, Table II). In most of the cases hydronephrosis was slight, only a few showing any considerable dilatation. The rapidity and completeness of the regression of the hydronephrosis after operation were independent of the degree of dilatation before operation.

In nearly 50 per cent of the cases pelvic tumors produced an extrinsic pressure defect on the dome of the distended urinary bladder, but this is not an unusual roentgenographic observation. In a large number of the postoperative roentgenographic examinations the same defect was still present

TABLE II.—ABNORMAL UROGRAMS

Preoperative hydronephrosis and postoperative normal roentgenogram	37
Right side dilatation	12
Left side dilatation	3
Bilateral dilatation	22
Operative damage	5
Preoperative and postoperative hydronephrosis	4
Urinary calcification	3
Total	49

and it is difficult to ascribe a cause for the persistence of this deformity.

The incidental roentgenologic findings not associated with genitourinary conditions were as follows: cholelithiasis in 3 cases; rheumatoid spondylitis in 2; Paget's disease in 2; splenomegaly in 2; bilateral coxa vara in 1; and bilateral congenital dislocation of the hip in 1 case.

The pyelograms after operation show that the ureter was injured 5 times, an incidence of 2.5 per cent. The injuries were detected after 3 abdominal hysterectomies and 2 vaginal hysterectomies. The right ureter was injured twice and the left 3 times. Thus, our experience coincides with others that the ureter is quite often accidentally injured.

In our series the resulting obstruction was only a temporary occurrence in 2 out of 5 cases. The reason for this temporary obstruction is difficult to assess accurately but it may be conjectured that it is due to dissolution of absorbable catgut, release of tension in nearby structures, or spontaneous recovery from a crushing injury.

The treatment of ureteric injury depends upon whether the results of obstruction continue. Sometimes improvement is shown without active treatment, and therefore a policy of watchful expectancy may be adopted. If, however, the obstruction shows no amelioration or there are other urinary tract complications operative treatment is indicated.

The most alarming feature of this type of ureteric injury is the innocuous symptomatology, and in all 5 cases it is doubtful whether the injuries would have been discovered if pyelography had not been used.

SUMMARY

1. Intravenous pyelography was performed on 200 consecutive patients before and after hysterectomy.

2. The preoperative pyelograms revealed an unsuspected high incidence of urinary tract abnormality.

3. The postoperative pyelograms showed a 2½ per cent incidence of ureteric injury as a direct result of the operation.

4. The ureteric injuries sustained were asymptomatic and would not have been discovered without the use of pyelography.

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THE ROLE OF THE SURGEON IN THE PROLONGATION OF UNCOMPLICATED SURGICAL CONVALESCENCE

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THE TOTAL DURATION of uncomplicated surgical convalescence is usually determined not by the patient's physiologic or psychologic needs, but by the surgeon's opinion. This conclusion is supported by: (1) the high correlation of the surgeon's forecast duration of convalescence with the actual duration of uncomplicated convalescence in this study; (2) the statement of most patients in this study that their surgeons determined the duration of their convalescent period; (3) evidence that patients who follow their surgeons' recommendations for a short convalescence feel as well at the time they return to work as those who follow the surgeons' recommendation for a long convalescence; (4) the wide range of opinion among surgeons concerning the proper duration of uncomplicated convalescence in the same hypothetic postoperative case; (5) the wide range of actual duration of convalescence within the same age group after the same type of operation; (6) the demonstrated safety of considerably shorter convalescent periods than those usually recommended; (7) the relatively short duration of altered metabolism following common uncomplicated surgical procedures; (8) the relatively short time for a properly sutured clean abdominal incision in animals to return to preoperative tensile strength; (9) the short convalescent period of domestic animals.

These facts demonstrate that the majority of individuals are advised to undergo far longer convalescence after common surgical procedures than is necessary, and, as a result of this advice, do so. This results in unnecessary iatrogenic "illness," considerable inconvenience, and economic loss to the individual and the nation.

This study was made to determine the relationship of the doctors' recommended (forecast) duration of postoperative convalescence to the actual duration and to the degree of disability at the time of returning to work. The convalescent period was considered to extend from the day of operation until the patient returned to work.

METHODS

Observations were made in the dispensary of an eastern industrial firm from May 1, 1957 until December 1, 1958. Employees were examined by a surgeon (N.H.M.) one or more times after certain surgical operations during the posthospitalization convalescent period. The degree of disability was estimated at each visit. A trained interviewer obtained sociologic and personal data from the patient and from the insurance forms. The data were recorded on a "Surgical Convalescence Study" form.

Clinical material. One hundred and seventy-five men and women were followed up during the posthospitalization convalescent period. Twenty-five, 14 per cent, of the 175 patients were not included because of significant "complications" which continued into, or appeared during, the posthospitalization period. Fifty-seven without postoperative complications were omitted from this part of the study because: (1) no forecasts were made available by the doctor in

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TABLE I.—ACTUAL CONVALESCENT PERIOD VERSUS THAT FORECAST BY DOCTOR IN 93 PATIENTS WITH UNCOMPLICATED CONVALESCENCE

			Convalescent period						
			Median, days		Average and range, days		Per cent of patients		
Operation	*No. of patients*	*Mean age, years*	*Actual*	*Forecast*	*Actual*	*Forecast*	*Actual equals forecast*	*Within 10 per cent of forecast*	*Prediction span, days*
Ing. herniorrhaphy	27 (M)	52	45	46	44.4 (20–73)	48.7 (21–91)	26	59	36 (17–90)
Appendectomy	15 (13-M) (2-F)	33	35	40	39.7 (21–79)	44.7 (28–91)	47	67	33 (19–78)
Hemorrhoidectomy	11 (10-M) (1-F)	42	26	33	29.9 (21–47)	33.1 (17–46)	18	55	27 (19–42)
Cholecystectomy	16 (5-M) (11-F)	42	53	56	58.3 (24–102)	56.8 (24–89)	50	75	37 (17–56)
Salpingo-oophorectomy	8 (F)	27	56	49	49.1 (24–66)	50.8 (24–78)	38	75	38 (19–53)
Hysterectomy	16 (F)	39	60	64	68.3 (45–103)	66.6 (44–94)	6	25	53 (27–106)

Convalescent period—days from operation to return to work, actual and that forecast by attending doctor (90 per cent were surgeons).
Prediction span—days from date on which forecast was made to the date forecast as day to return to work.

22; (2) the prediction span was less than 17 days in 20; (3) the date on which the forecast was made was not shown in 15; therefore, the prediction span could not be calculated. Thus, there were 93 patients without postoperative complications for whom a forecast of the convalescent period was made. Sixty-five of the 93 patients were hourly employees (45 men and 20 women) and 28 were salary employees (10 men and 18 women).

Surgical operations selected for study. The common operations chosen for study (Table I) are relatively limited in extent and are usually not preceded by debilitating illness or significant loss of weight. Thus, the duration of convalescence in each of these patients probably reflects the actual time required for physiologic and psychologic recovery from the operation or the "beliefs, customs, and desires" of the doctor and patient concerning the duration of convalescence.

Patients with a diagnosis such as "regional ileitis," often a debilitating illness, with "appendectomy" as the operation recorded by the surgeon on the insurance form, or multiple operations performed at different times during the same illness episode were not included. If the patient had two operations such as a cholecystectomy and appendectomy at the same time, the case was included in the study and coded under cholecystectomy, the operation with the longer convalescence.

Forecast duration of convalescence. The term "forecast" is used for the number of days which the doctor forecast—advised or recommended—for convalescence from the day of operation to return to work. The term "prediction span" indicates the number of days from the date on which the doctor made his forecast to the date which he predicted as the day for returning to work. Patients with prediction spans of less than 17 days were not included in this analysis.

In 74 per cent of the 93 patients in this series the attending surgeon's or physician's forecast convalescence was written on the accident and sickness disability claim form. In 26 per cent the information was a verbal report by the patient of the doctor's recommendation. The patient's verbal report of the doctor's forecast was the same as that written on the insurance form by the doctor in the 12 cases in which both were obtained. This fact suggests that the verbal reports were usually accurate.

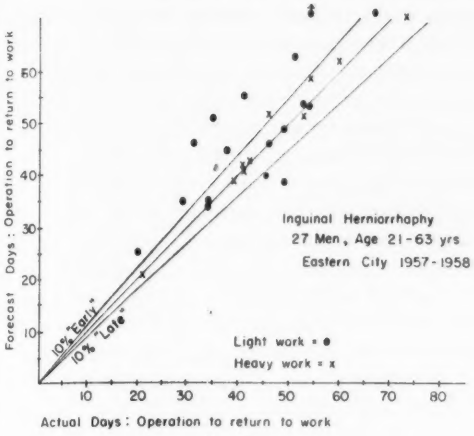
Forecast Days : Operation to return to work
Actual Days : Operation to return to work
Inguinal Herniorrhaphy
27 Men, Age 21-63 yrs
Eastern City 1957-1958
Light work = ●
Heavy work = x
10% "Early"
10% "Late"

FIG. 1.

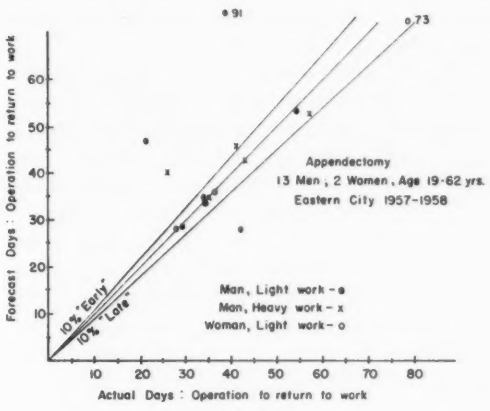
Forecast Days : Operation to return to work
Actual Days : Operation to return to work
Appendectomy
13 Men, 2 Women, Age 19-62 yrs.
Eastern City 1957-1958
Man, Light work - ●
Man, Heavy work - x
Woman, Light work - o
10% "Early"
10% "Late"

FIG. 2.

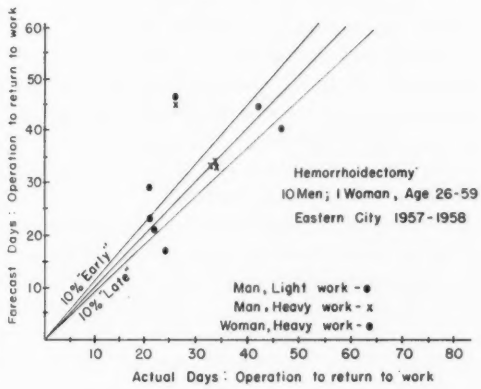
Forecast Days : Operation to return to work
Actual Days : Operation to return to work
Hemorrhoidectomy
10 Men; 1 Woman, Age 26-59
Eastern City 1957-1958
Man, Light work - ●
Man, Heavy work - x
Woman, Heavy work - ●
10% "Early"
10% "Late"

FIG. 3.

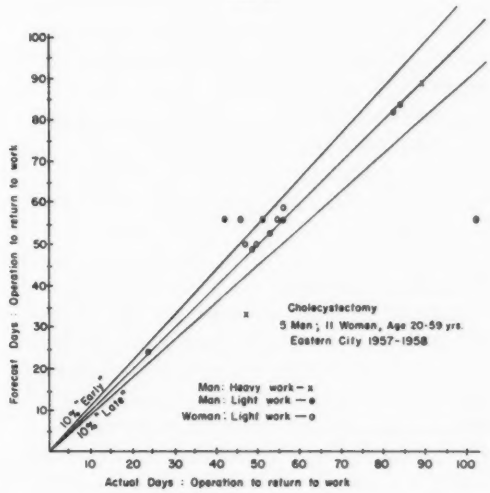
Forecast Days : Operation to return to work
Actual Days : Operation to return to work
Cholecystectomy
5 Men; 11 Women, Age 20-59 yrs.
Eastern City 1957-1958
Man: Heavy work - x
Man: Light work - ●
Woman: Light work - o
10% "Early"
10% "Late"

FIG. 4.

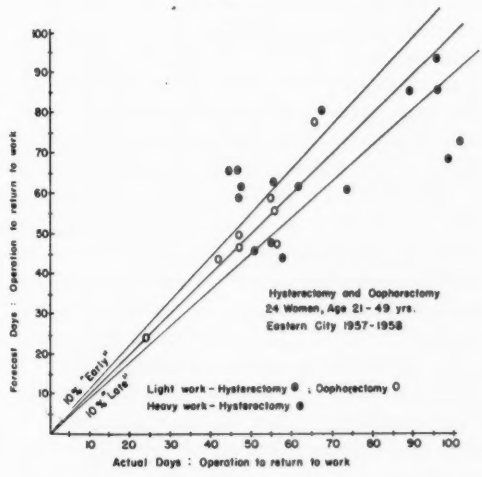
Forecast Days : Operation to return to work
Actual Days : Operation to return to work
Hysterectomy and Oophorectomy
24 Women, Age 21-49 yrs.
Eastern City 1957-1958
Light work - Hysterectomy ● ; Oophorectomy O
Heavy work - Hysterectomy ●
10% "Early"
10% "Late"

FIG. 5.

FIGS. 1 to 5. Scatter diagrams illustrating the close correlation between the doctor's forecast or recommended duration of convalescence and actual duration of uncomplicated convalescence. Patients returning within ±10 per cent of the forecast time are considered to have returned at the time forecast.

Assessment of disability. Each patient was examined one or more times during the posthospitalization period. At these times, the reviewing surgeon made an estimate of the individual's subjective state of health related to the state of health prior to the illness requiring surgery, his present "absolute" estimate of well-being, appetite, nervousness, and so forth. If a complication,

for instance a history of influenza, was evident, the patient was followed up but not included in this series.

The "disability score" was obtained by evaluating separately the severity of the subjective symptoms of spontaneous pain, pain with effort, spontaneous fatigue, fatigue with effort, and weakness. These were each scored 0 to 3 points (none = 0, slight = 1, moderate = 2, severe = 3). The frequency of the same symptoms was also scored 0 to 3, and the points summed. The maximum possible points for subjective symptoms was 30. To this was added the summed objective disability score of 0 to 3 for incisional tenderness, incisional hernia, and incisional infection. Thus a maximum total of 39 disability points was possible. A score less than 7 represents minimal symptomatology and findings, (e.g., slight incisional tenderness = 1, slight spontaneous incisional pain = 1, occurring once or twice a week = 1, and mild afternoon fatigue after working around the house = 1, every day = 2; total = 6).

RESULTS

Surgeon's forecast duration of convalescence versus actual duration. Forecasts were made in 90 per cent of the 93 cases by the operating surgeon. A total of 56 surgeons made 84 forecasts and 9 attending physicians made 9 forecasts. Fifty-four per cent of the surgeons were certified by the American Board of Surgery.

Table I and Figures 1 to 5 show the relationship of the surgeons' forecasts to the actual durations of uncomplicated convalescence after inguinal herniorrhaphy, appendectomy, hemorrhoidectomy, cholecystectomy, hysterectomy, and oophorectomy.

Thirty per cent of all convalescents returned on the exact day forecast. A total of 58 per cent returned to work within 10 per cent of the forecast time even though the forecasts were made many weeks before. These patients are considered to have ended convalescence at the time forecast. Thus, it can be concluded that the surgeons' forecasts even though varying widely in each operative group were remarkably accurate estimates of the time needed by these patients for physiologic and psychologic recovery from operation, or that the forecasts (recommendations) influenced the duration of convalescence. Fifty-two patients were questioned on this subject after they returned to work. Of these, 64 per cent stated that the opinion of their doctor determined the actual time of return to work, while 29 per cent believed they decided the time and in 7 per cent it was the plant physician.

Disability at end of convalescent period. The relationship of the length of the recommended convalescent period to the degree of disability has been estimated. Table II shows the "disability scores" within about 1 week prior to return to work. Those individuals returning earlier than the median forecast for their particular operative group (e.g., appendectomy) had approximately the same distribution of scores as those returning later than the median (Table IIA). It thus appears that the short convalescent periods in the group as a whole were associated with approximately the same degree of disability near the end of the convalescence as those with long convalescent periods. This fact might suggest that the patients returned to work when they felt in satisfactory condition to do so. However, most patients returned to work when their doctors had forecast even though these forecasts had been made 17 to 106 days before the patient returned to work.

The distribution of the disability scores of those who followed the doctor's forecast (Table IIB) is about the same whether the forecast time was short, earlier than the median forecast, or long, later than the median forecast. This observation would suggest that the doctor's forecast, as a prognosis of how the patient would feel at the time of return to work, is surprisingly accurate or that his forecast affects either the rate of convalescence or the expressed feelings of the individual at the time he returns to work. On the other hand, individuals

who returned earlier to their work than forecast by their doctor (Table IIC, line 1) had lower disability scores than those who returned at the forecast time (Table IIB), or those who returned later (Table IIC, line 2). This observation suggests that those returning earlier than recommended tended to minimize or actually have fewer symptoms. It also suggests that those individuals who returned earlier than recommended did not push themselves unduly.

TABLE II.—DURATION OF CONVALESCENCE AND "DISABILITY SCORE"

Convalescence	Disability score: 0	1–4	5–7	8–10
	Per cent of sample			
A. All patients (74)				
1. Shorter than median forecast for operative group (40)	50	37	8	5
2. Longer than median forecast for operative group (34)	53	29	9	9
B. Patients within 10 per cent of individual forecast (41)				
1. Shorter than median forecast for operative group (23)	43	39	9	9
2. Longer than median forecast for operative group (18)	44	39	11	6
C. Patients not within 10 per cent of individual forecast (33)				
1. 10 per cent earlier than individual forecast (19)	74	21	5	0
2. 10 per cent later than individual forecast (14)	50	29	7	14

74 patients had disability scores determined within one week of return to work (see text for scoring).
Median forecast for each operative group (e.g., cholecystectomy).
In Section C, the duration of convalescence for each individual was compared with the doctor's forecast for him.

DISCUSSION

The data presented in the foregoing indicate that most patients (as expected) follow the recommendation of their surgeon as to the duration of the uncomplicated postoperative convalescent period and that those following the recommendations for a short convalescence do not have more disability at the time of their return to work than those following a recommendation for a long convalescence.

It seems possible that the 3 or 4 fold range of recommendations noted in this study may be due to the accuracy of the surgeon in assessing the time required for various postoperative patients to get well. On the other hand, the wide range may result from an intrinsic variation of surgical opinion because of the inadequate criteria for forecasting the duration of convalescence.

Since the patients following the recommendation for a short convalescence have no greater disability than those following recommendation for a long convalescence, it seems possible that a surgeon's forecast of a long convalescence may influence the feelings of the patient and tend to decrease the physical activity necessary for reconditioning. This possibility needs exploration since preliminary evidence indicates lesser activity in those patients for whom the surgeon had forecast a long convalescence.

This discussion will review: (1) the variation in the surgeon's opinions in the same hypothetic cases, (2) some of the statistical data indicating the duration of postoperative convalescence in various groups, and (3) data indicating the relatively short time necessary for healthy men and domestic animals to return to a normal physiologic state after surgical trauma.

The wide range of opinion about the optimum duration of convalescence. There is a wide range of opinion among surgeons, industrial physicians, and general practitioners concerning the proper duration of uncomplicated postoperative convalescent period in the same hypothetic "otherwise healthy patient of normal weight," as pointed out by Moss and associates. Table III shows the average opinions and ranges of a nation-wide sample of diplomates of the American Board of Surgery concerning the number of days necessary after various operations before return to specified work. A similar wide distribution of opinion was found in the three other physician groups surveyed. The wide range of opinion is not due to a few individuals. It is apparent that no adequate criteria for termination of the optimum postoperative uncomplicated convalescent period have been established. Beck and Rapp (4) came to a similar conclusion as a result of their pioneering study.

The duration of the surgical convalescent period in men. The average duration of con-

TABLE III.—OPINIONS OF SURGEONS REGARDING DURATION OF CONVALESCENCE

Operation	*Age, years*	*Work*†	*Time believed necessary, days** — *Average*	— *Range*
Inguinal herniorrhaphy	25	Light	18.9	7–42
	25	Heavy	47.9	21–168
(Indirect hernia)	50	Light	21.1	7–56
	50	Heavy	53.8	28–168
Appendectomy	25	Light	13.2	3–28
(McBurney)	25	Heavy	27.7	7–75
Hemorrhoidectomy	40	Light	12.6	2–42
	40	Heavy	21.1	2–49

Opinions of 77 surgeons certified by the American Board of Surgery (10).
*Days from operation to return to work. It was assumed that (a) the patient was a healthy man of normal weight and (b) the convalescence uncomplicated.
†Light work: sitting, e.g., desk job or assembly of small parts. Heavy work: lifting 20 to 35 pounds at relatively short intervals or heavier object 1 or more times per day, climbing, pushing heavy objects, operating heavy foot pedals, jumping, or running.

TABLE IV.—POSTOPERATIVE CONVALESCENCE

	Average duration—Men, days — *Herniorrhaphy*	*Appendectomy*	*Hemorrhoidectomy*
U. S. Air Force 1956 (Gold)	13.0	12.3	10.1
Naval Training Station 1956 (Spoont)	21.9	—	—
U. S. Air Force 1954, age 20–29 (Wenger)	16.4	12.1	12.8
Industrial Employes, age 20–29 Insurance data 1957 (Saffeir)	42	37	22
Clerks, supervisors 1949–1953 (Powers)	21.0*	—	—
Farmers 1949–1953 (Powers)	28.0†	—	—
Sedentary 1956 (Bartels and Johnston)	24.7	—	—
Standing, walking (Bartels and Johnston) 1956	29.1	—	—
Moderately heavy work (Bartels and Johnston) 1956	33.6	—	—
Heavy work (Bartels and Johnston) 1956	33.9	—	—
Industrial salary employes 1956 (Fleming)‡	32.0	25.0	22.8
Industrial wage employes 1956 (Fleming)‡	40.1	30.3	26.1
Industrial employes 1957 (Saffeir)	46	35	28
Auto workers, Pontiac, Mich., 1921–1922 (Brundage)	49.1	35.7	—

*Known recurrences—none in 45 hernias of all types.
†Known recurrences—1 in 54 hernias of all types.
‡Special efforts are made to encourage earlier return to work in this company.
Brundage data quoted by Fleming.

valescence after herniorrhaphy, appendectomy, and hemorrhoidectomy in the Air Force is from one-half to one-third that in civilian males of about the same age distribution, as shown by Wenger and Gold. Table IV summarizes this and other data from various groups. From the data of Spoont, it is seen that men at a Naval Training Station returned to vigorous physical training after hernia repair in about one-half the time—shown by Saffeir—that civilian men, 20 to 29 years old, convalesced before return to work.

A short convalescence is not confined to the Military Services. John Powers has reported that his patients after hernioplasty, if clerks, supervisors, and the like, returned to their work in an average of 21 days and farmers to heavy farm labor in 28 days.

Bartels and Johnston in a study of patients from several Detroit hospitals reported return to sedentary duties in 24.7 days compared to an average of 33.6 days for those returning to moderate exertion, and 33.9 days for those whose work required quite heavy exertion. All groups showed a wide range, e.g., 7 to 84 days for the moderately heavy work group. They concluded from this and studies of other patients subjected to hernia repair that "there was little correlation between the rigors of a man's occupation and the time he returned to work."

The last two lines of the Table IV give evidence that the average durations of convalescence after herniorrhaphy and appendectomy have not decreased in almost 40 years despite early ambulation and great advances in surgical practice.

Air force experience versus civilian opinion and practice. The duration of convalescence after appendectomy in the Air Force is compared in Figure 6 to that of 43 civilian men aged 20 to 29 years. The median time for return to full duty in the Air Force was 9 days while that in the sample of men in industry was 31 days. Fifty per cent of the men in the Air Force were back to full duty by the time that the first man in this civilian group returned to work on the ninth day of convalescence.

Figure 7 shows the data from the opinion survey of civilian doctors regarding the time necessary for an otherwise healthy young man of 25 to return to light and to heavy work after appendectomy. The cumulative frequency curves show the per cent convalescing if 1 patient were to follow the

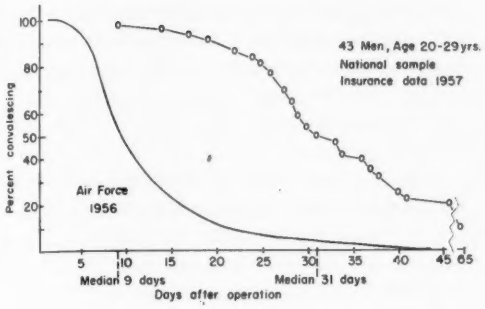

FIG. 6.

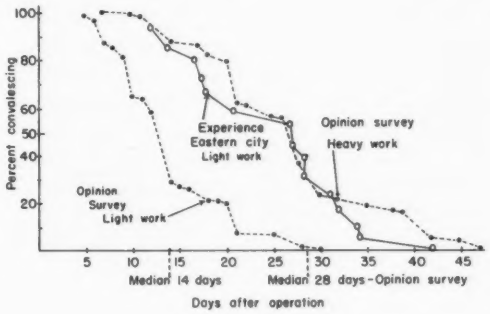

FIG. 7.

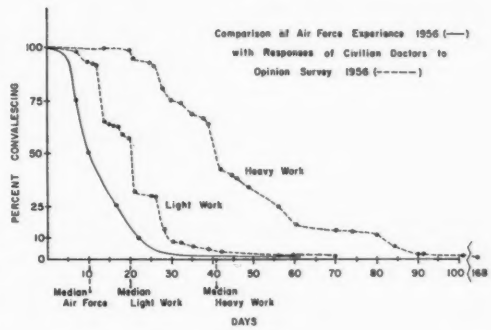

FIG. 8.

FIG. 6. The cumulative frequency curve showing the days from operation to return to full duty in the Air Force as a "smoothed" curve of the graphic data presented by Gold. This is compared with the cumulative frequency curve of the times from appendectomy to return to work of men aged 20 to 29 years from the data of Saffeir.

FIG. 7. Cumulative frequency curves showing the duration of uncomplicated convalescence for 15 men, aged 20 to 36 years (average 26 years) who returned to light work after appendectomy. The results of an opinion survey of civilian doctors (N=220) are plotted for comparison. The hypothetic subject of the survey was assumed to be an otherwise healthy 25 year old man of normal weight. Light and heavy work are defined in a footnote to Table III.

FIG. 8. Cumulative frequency curves showing that the actual duration of convalescence after inguinal herniorrhaphy in the Air Force is considerably less than the time considered necessary by 228 doctors replying to a questionnaire. The hypothetic subject of the opinion survey (10) was assumed to be a healthy 25 year old man of normal weight.

opinion of each of the 220 doctors answering the question. These data are compared with the actual time of return to light work by 15 young men (in this study) after uncomplicated convalescence. The median time for these men with uncomplicated convalescence to return to light work was 3 times that of the Air Force experience shown in Figure 6, and the frequency curve approximates that of the opinion survey for heavy work. The median opinion for return to light work is over half again as long as the median in the Air Force experience (Fig. 6).

The doctors' opinions about return to light work and to heavy work after uncomplicated convalescence from inguinal herniorrhaphy in a healthy young man are plotted as cumulative frequency curves in Figure 8. The Air Force experience, which includes patients with postoperative complications, is given for comparison. The median duration of convalescence recommended in the hypothetic case before return to light work was 20 days; that before return to heavy work was 41 days. In the Air Force experience the actual median time before return to full duty was 10 days.

It is thus apparent (Figs. 6, 7, 8, and Tables III and IV) that the opinion of civilian doctors as to the time necessary for uncomplicated convalescence from inguinal herniorrhaphy and appendectomy in healthy young men is far longer than the actual convalescence experienced in Air Force personnel.

Recommendations to patients in this study versus the opinion survey. Figure 9 shows the responses of 77 surgeons, certified by the American Board of Surgery, when asked about the time believed necessary for an

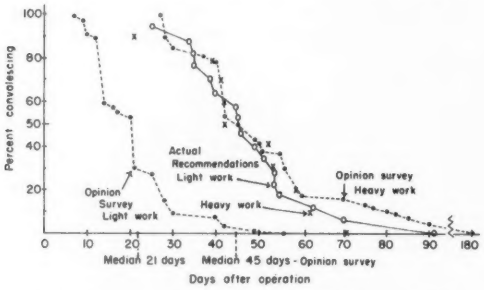

FIG. 9. Cumulative frequency curves indicating the similar distribution of actual recommendations of surgeons for men (average age 52 years) returning to light (17) and to heavy (10) work after repair of indirect, direct, recurrent, and bilateral hernias. These are compared with the results of an opinion survey (10) of a nationwide sample of diplomates of the American Board of Surgery (N = 77) in a hypothetic case of a healthy man aged 50 years subjected to repair of an indirect inguinal hernia.

otherwise healthy man, 50 years of age, to convalesce from repair of an indirect inguinal hernia before returning to defined light or heavy work. The actual times recommended or forecast by the surgeons of the patients in this study for their return to similarly defined light and heavy work after inguinal hernia repair of all types are plotted for comparison. The recommendations for return to light work and those for return to heavy work follow the frequency curve of the responses to the heavy work question in the survey. Although the variation in types of hernia repaired may account for some of the variations in opinion, it seems probable from the similarity of light and heavy work curves that there was inadequate consideration given to the type of work to which the patient was to return.

The similarity of the frequency curves for the duration of convalescence (Fig. 7) and for recommended duration (Fig. 9) to the frequency curves of opinions strongly suggest that intersurgeon differences of opinion rather than interpatient differences in condition are the major factor in determining the variations in duration of uncomplicated convalescence.

TABLE V.—CONVALESCENT PERIOD AFTER INGUINAL HERNIORRHAPHY IN MEN

	No. of men	*Days* — *Average*	*Range*
Time determined by doctor	37*	39.5	21–70
Patient told to return to work when he felt able	42†	20.5	5–70

*Three hernias recurred.
†No recurrences.
Adapted from the data of Bartels and Johnston.

The short duration of disturbed metabolism following common surgical procedures. Experimental and other data including clinical experience indicate that metabolic abnormalities do not account for the many weeks commonly recommended as periods of convalescence from appendectomy and herniorrhaphy and similar operations in the nondebilitated individual.

The metabolic pattern of uncomplicated convalescence following surgical procedures such as those studied by us has been well described by Moore, Hardy, and others. The postoperative changes in electrolyte, water, and nitrogen metabolism of such patients usually return to normal within a week after operation. Similarly, the increased activity of the adrenal cortex and medulla usually subsides within 4 to 7 days in the absence of fever or other continuing stress.

Taylor and Keys have reported that return to baseline physical stamina by healthy men after 3 weeks in bed required 3 to 5 weeks while 2 days of acute starvation required only 48 hours of recovery despite a greater nitrogen loss in the latter. The usual inactivity of the posthospitalization period of convalescence apparently leads to loss of stamina. Graduated activity in the convalescent period after febrile disease has been reported by Rusk to decrease the duration. Beck (3) recommends the prescription in writing of a regimen of graduated postoperative activity.

The short time required for incisions to return to preoperative tensile strength. The classical report of Howes, Sooy, and Harvey established the fact that clean incised wounds of the skin, intestine, and fascia of dogs return to approximately 100 per cent of normal tensile strength in 12 to 14 days. Royster and associates have reported similar data in

exercised and nonexercised dogs. The data reported by Allam and Martin indicate the acceptance of this time in veterinary practice. There appears to be no satisfactory data on the tensile strength of abdominal incisions in humans. However, the Air Force experience and that of others would appear to justify the general extension of this concept to humans who have not suffered a debilitating illness, postoperative complications, or degenerative disease.

The short convalescence of domestic animals. Allam and Martin have reported that surgical convalescence in animals is characterized by rapid return to full activity. Dogs such as greyhounds return to competitive racing in 2 weeks after total hysterectomy and race horses are in full training, including jumping, 4 weeks after ventral herniorrhaphy.

The short duration of the patient-determined convalescent period. Bartels and Johnston have reported that men, after inguinal herniorrhaphy, "who were permitted to return to work when they felt able lost only half as much time from the job as those whose return was governed by a physician" (Table V). They stated that this held true regardless of job classification. The 3 recurrences of hernia were in the group whose return to work was "governed by a physician."

SUMMARY AND CONCLUSION

Certain practical conclusions seem evident:

1. The opinions of surgeons regarding the proper duration of the uncomplicated postoperative convalescent period in otherwise healthy men and women vary widely.

2. The surgeon's recommendation is the major determinant of the total duration of uncomplicated convalescence in most patients.

3. Most otherwise healthy patients do not need the prolonged period of postoperative convalescence usually recommended.

It is suggested that the patient undergoing an uncomplicated convalescence be directed to increase his activities gradually to his usual level and return to his work when he feels fit to do so. The patient should visit the surgeon's office early in the posthospitalization period and prior to return to work to permit detection of objective findings that might contraindicate further increase in activity or return to work. A specific forecast or recommendation concerning the duration of convalescence should not be made. Fears of the patient or doctor regarding shorter periods of convalescence should be re-evaluated in the light of the experience of the Air Force and others.

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THE DIRECT REMOVAL OF PORTAL BLOOD AMMONIA BY THE LIVER

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SINCE 1930 when Bollman and Mann described elevation of blood ammonia after hepatectomy in dogs, the relationship of ammonia to liver disease, including cirrhosis, hepatic coma, and after surgical portal-systemic shunts has been extensively studied.

Experimental evidence at the present time offers strong support to the theory that the normal liver with a normal blood flow can remove a large amount of ammonia from portal blood in one passage. McDermott and his associates catheterized the portal and hepatic veins in normal subjects and found that the blood leaving the liver contained only one-third the ammonia concentration present in the portal vein. Furthermore, it has been shown that, in shunting of portal blood or in severe liver damage, accumulation of ammonia frequently occurs in toxic concentrations and that clearance of blood ammonia by the liver may fail. It was decided, therefore, that studies of hepatic vein ammonia concentration rather than peripheral concentration alone would be more significant in determining the ability of the liver to remove this substance.

In the present study, hepatic inflow and outflow concentrations of blood ammonia were measured during the infusion of ammonium salts into the portal system to determine the ability of the liver to clear ammonia in varying experiments in the dog.

METHODS

Adult mongrel dogs weighing between 10 and 25 kilograms were anesthetized with 30 milligrams of intravenous sodium pentothal or pentobarbital per kilogram of body weight. Blood pressures were monitored with a mercury manometer attached to a femoral artery cannula. Through a long midline abdominal incision, 4 fine polyethylene catheters were placed for venous sampling and ammonia infusion (Fig. 1). One catheter was threaded through a splenic vein to the bifurcation of the portal vein at the porta hepatis. Another catheter was introduced into the free segment of the left interlobar hepatic vein and secured with a fine pursestring suture. The end of this catheter was passed into the vein 1 to 2 centimeters and directed away from the suprahepatic vena cava, avoiding both a hepatic wedge sample and a sample mixed with blood from the vena cava. The position of this catheter was judged critical and was verified at the conclusion of every experiment. A third catheter was placed in the femoral vein and passed proximally into the lower inferior vena cava. A fine catheter used for ammonium chloride infusion was placed in a distal ileal vein. The abdominal catheters were carried out through stab wounds and secured to the skin. The incision was closed, no further anesthetic was given, and all studies were performed when the animals appeared to stabilize after operation.

A 1 per cent ammonium chloride solution was given by a calibrated Bowman constant infusion pump through the catheter previously placed in the mesenteric vein of the distal ileum for a 20 minute period. Blood samples were taken for ammonia concentration at intervals before, during, and after the infusion. Whole blood ammonia determinations were performed according to

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a modification of the method of Seligson and Hirahara.

Four experimental groups of animals were studied as follows: Eighteen experiments were carried out in normal dogs in group 1, using varying infusion rates. In group 2, 10 infusion studies were performed immediately after hepatic arterial inflow occlusion accomplished by ligation of the hepatic artery and its gastroduodenal branch to prevent collateral arterial inflow. In group 3, 7 experiments were performed in dogs after partial hepatectomy. The left, middle, and omental lobes of the liver were completely removed, which resulted in approximately a 70 per cent hepatectomy. This percentage was determined by weighing the amount of liver removed and the residual liver at autopsy. In the 9 experiments in group 4, dogs were administered an average of 20 cubic centimeters of carbon tetrachloride 3 times a week by gastric gavage until hepatic dysfunction became severe, as evidenced by anorexia, weight loss, icterus, prolonged prothrombin time, and increased bromsulphalein retention. At the time of the infusion studies, liver biopsies were performed to obtain histologic evidence of the liver damage.

RESULTS

In normal control dogs fasted for 24 hours, the mean ammonia concentration in the portal vein was 4.0 ± 1.1 gamma of ammonia nitrogen per cubic centimeter of whole blood. The simultaneous mean hepatic vein concentration was 1.9 ± 0.5 gamma per cubic centimeter, and the systemic venous concentration was 1.9 ± 0.5 gamma per cubic centimeter. When ammonium salt solutions were infused into the animals, the portal levels recorded were all above initial values. In Figure 2 a typical experiment in group 1 is depicted, showing the resultant concentrations of ammonia in the portal, hepatic, and systemic veins before, during, and after infusion.

The large rise in portal ammonia during infusion was accompanied by similar but smaller changes in the hepatic vein ammonia. As is seen in this experiment, the ammonia in the hepatic vein remained at preinfusion levels until the portal ammonia level exceeded 18 gammas per cubic centimeter. To obtain this portal level an infusion rate of over 400 gammas of ammonium chloride nitrogen per kilogram of body weight per minute was required. Ten minutes after the termination of the infusions all venous ammonia concentrations were at or approached the preinfusion levels.

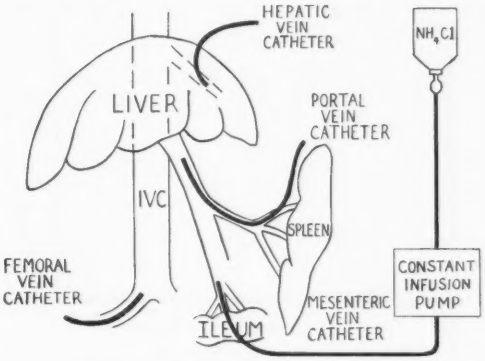

FIG. 1. The experimental preparation.

To correlate all experiments in group 1 a

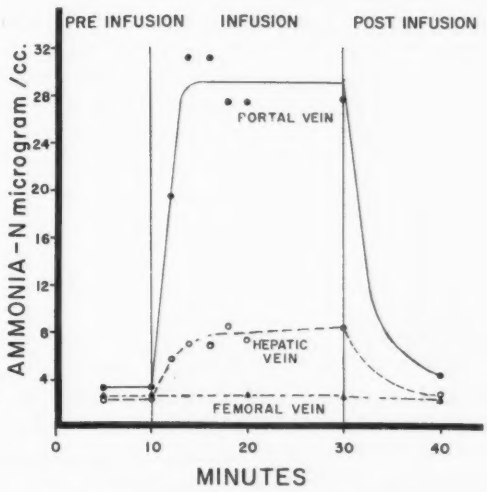

FIG. 2. Results of experimental infusion of 1 per cent ammonium chloride solution into the ileal vein of a normal dog at the rate of 580 gammas of ammonium nitrogen per kilogram per minute.

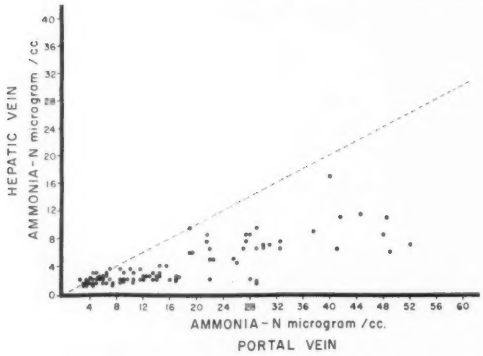

FIG. 3. Scattergram of 218 simultaneous portal and hepatic vein ammonia determinations in group 1. Broken line indicates level of 50 per cent clearance by the liver.

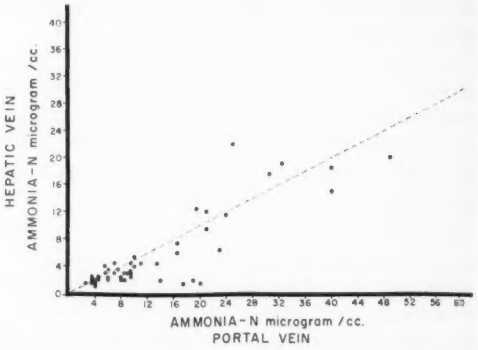

FIG. 5. Results of 100 simultaneous portal and hepatic vein ammonia determinations in group 3 dogs after partial hepatectomy.

scattergram comparing portal and hepatic vein ammonia levels is presented (Fig. 3). Simultaneous portal and hepatic vein samples during the experiments are included, showing the effect of increased portal ammonia on hepatic vein ammonia levels. It is apparent in this group of normal dogs that the liver was able to remove approximately 80 per cent of the portal blood ammonia. In no experiment was the reduction less than 50 per cent, as indicated on the scattergram by the broken line.

The group 2 infusion studies after hepatic arterial inflow occlusion are shown in Figure 4. In this group the removal of portal blood ammonia by the liver was similar to that in the normal dogs. The mean reduction of portal ammonia was 90 per cent, and no value was below 50 per cent. These values did not differ significantly from those in the normal control animals.

The results in the group 3 animals after a 70 per cent partial hepatectomy are shown in Figure 5. In this group the ammonia reduction was less and approximated 50 per cent of the portal level.

The dogs in group 4, given carbon tetrachloride, showed evidence of severe liver damage in a rather short period. Within 3 to 5 weeks they became anorectic and very weak, their weight loss averaged 25 per cent, liver function tests were abnormal, and the tissues appeared jaundiced at operation. Grossly the livers were firm, somewhat atrophic, and appeared to show areas of yellowish degeneration and necrosis. Histologic sections revealed absence of the normal cords of liver cells, fatty change, and necrosis with centrolobular neutrophilic infiltration and fibrosis.

The concentration of blood ammonia in all preinfusion samples in these animals was above that in the corresponding samples from normal dogs. In 1 animal, initial blood ammonia levels were 19.5 gammas per cubic centimeter in the portal vein, 14.8 gammas per cubic centimeter in the hepatic vein, and 13.6 gammas per cubic centimeter in the femoral vein. This animal showed evidence of severe liver damage and chronic ammonia toxicity.

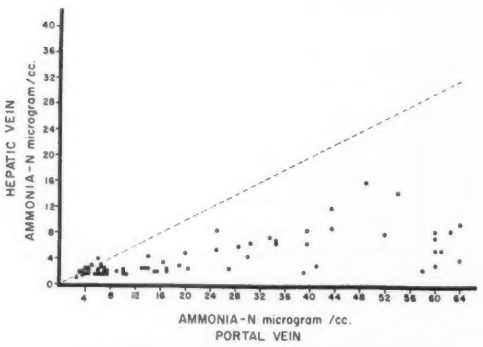

FIG. 4. Findings from 138 simultaneous portal and hepatic vein ammonia determinations in group 2 dogs with hepatic arterial inflow occlusion.

The effect of ammonium salt infusion into the portal system in this group is shown in Figure 6. There appeared to be considerable impairment in the clearance of ammonia even at very low infusion rates, and the high levels persisted for much longer periods than in the control group. The mean ammonia clearance in this group was only 38 per cent of the portal ammonia concentration.

In Figure 7, a comparison of the results in the 4 groups studied is shown with linear regression lines of the scattergram determinations previously represented for each group.

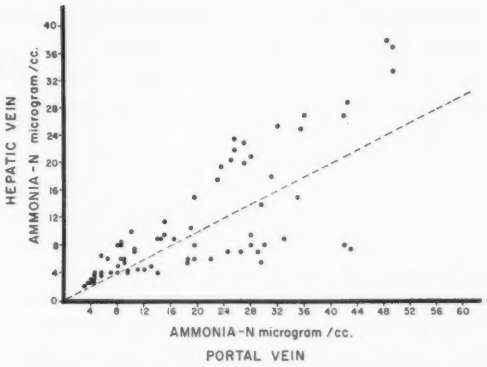

FIG. 6. Results in group 4 animals with carbon tetrachloride poisoning. Effect of increased portal vein ammonia on hepatic vein levels; 124 simultaneous determinations.

DISCUSSION

The experimental condition of acute elevations in portal blood ammonia for brief periods in these studies parallels the elevations noted in the portal blood after the ingestion of a heavy protein meal or ammonium salts or after rapid gastrointestinal hemorrhage in both animals and humans. Under conditions of controlled infusion of ammonia into the portal system, therefore, it was believed that a more physiologic response could be elicited and a better estimation of the hepatic clearance obtained.

Previous studies of blood ammonia changes after infusion of ammonium salts into the systemic veins have been complicated by the action of the extrahepatic tissues. Lawrence and his associates have shown that exogenously administered ammonia can be removed by extrahepatic tissues in eviscerectomized dogs in the face of rising ammonia levels in the blood stream. Artz and his coworkers have demonstrated that the concentration of blood ammonia entering tissues such as muscle or brain is greater than blood leaving these tissues and suggest that, when the systemic ammonia level is rising, the tissues can bind this ammonia and release it again when the level is decreasing. Presumably this phenomenon could be explained by rapid transamination in the extrahepatic tissues, although the exact mechanism is not clear. Bessman and Bessman have also shown differences in arterial and venous ammonia concentrations in patients with ammonia intoxication. It can be seen, therefore, that in a study of the metabolism by exogenous ammonia administration, other than into the portal system, these extrahepatic tissues act as an additional site of ammonia uptake. They must be considered, therefore, before acute changes in ammonia concentration can be attributed solely to the production of urea by the liver in the Krebs' ornithine cycle.

These studies confirm the fact that the liver, per se, can remove a large quantity of ammonia administered rapidly into the portal system. The amount necessary to exceed hepatic tolerance in normal animals and to

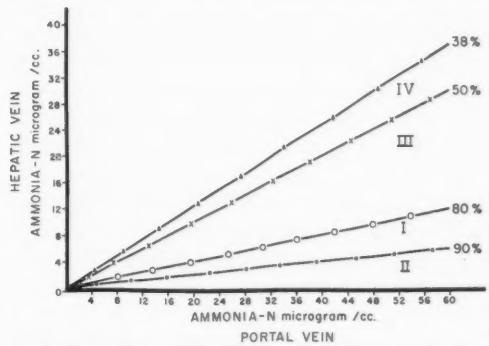

FIG. 7. Mean ammonia clearance in experimental groups. Linear regression analysis of ammonia clearance by all animals in each experimental group, plotting simultaneous portal and hepatic vein levels. Roman numerals indicate groups 1 to 4.

produce elevations in hepatic vein levels was greater than 400 gammas of ammonia nitrogen per kilogram of body weight per minute administered as the ammonium salt. Regardless of the rate of infusion, a portal blood ammonia level of 18 gammas per cubic centimeter or higher was necessary before any rise in the hepatic vein levels could be demonstrated. No significant difference in portal ammonia clearance by the liver could be demonstrated in animals with hepatic arterial occlusion, which suggests that the liver can handle ammonia normally, even under relatively anoxic conditions for the brief periods studied in these experiments.

Early in these experiments, partial hepatectomy of less than 70 per cent of the total liver mass did not significantly alter the ammonia removal rate. Only after complete removal of the left, middle, and omental lobes, leaving only the small right lobe, could any significant alterations be elicited, showing clearly the reserve capacity of the liver in handling this metabolite. This phenomenon has been clinically evident in humans, in that no case of ammonia intoxication has been reported to follow extensive removal of portions of the liver for neoplastic disease.

It was obvious, however, that the animals subjected to severe cellular necrosis with carbon tetrachloride had a greatly reduced capacity to remove ammonia from the portal system. The observation of spontaneous ammonia intoxication with elevated portal, hepatic, and systemic vein levels demonstrates that the liver could not handle even the ammonia produced by the animal itself in some of these studies. In any case, severe impairment of ammonia metabolism was noted in all animals in this group, indicating the diffuse cellular damage present.

SUMMARY AND CONCLUSIONS

1. A preparation has been described for measurement of hepatic inflow and outflow concentrations of ammonia. This method deals directly with the ability of the liver to clear an exogenously administered ammonium salt through the portal system and is not directly influenced by the uptake of ammonia by the peripheral tissues.

2. The normal portal blood ammonia concentration in fasting dogs was 4.0 gammas per cubic centimeter (standard deviation, 1.1). The simultaneous mean hepatic vein concentration was 1.9 gammas per cubic centimeter (standard deviation, 0.5), and the systemic venous concentration was 1.9 gammas per cubic centimeter (standard deviation, 0.5).

3. A portal level of over 18 gammas of ammonia nitrogen per cubic centimeter has been found necessary to exceed the ability of the liver to clear ammonia. The normal liver is able to remove 80 per cent or more of the ammonia concentration in the portal vein.

4. Hepatic arterial occlusion did not significantly alter the clearing of portal blood ammonia in the brief periods studied.

5. Partial hepatectomy reduced the ability of the liver to remove ammonia, but 70 per cent removal of the liver was necessary to produce this reduction.

6. Chronic carbon tetrachloride poisoning produced spontaneous ammonia intoxication in some animals and severely impaired the removal of ammonia by the liver in all animals.

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COLLATERAL PATHWAYS UTILIZED UPON LIGATION OF THE INFERIOR VENA CAVA AT DIFFERENT LEVELS IN THE DOG

O. W. OUGHTRED, M.D., and S. R. M. REYNOLDS, Ph.D., D.Sc., Chicago, Illinois

MANY ARTICLES have been published on the problem of treatment and management of venous thrombosis and pulmonary embolism. There is no agreement, however, regarding the best therapy, the etiology of these conditions, or the best prophylactic measures. Nevertheless, interest has increased in recent years in operative intervention by venous ligation. During the last decade, there have been French, Polish, Russian, and South American contributions to the literature on the rationale, plausibility, and results of ligation of the inferior vena cava for the treatment of advanced chronic cardiac insufficiency. The rationale for this operation cannot be properly divorced from certain basic anatomic and physiologic considerations.

POSSIBLE COLLATERAL PATHS IN INFERIOR CAVAL LIGATION

The collateral connections, taken as a whole, that are available when the inferior vena cava is ligated inferiorly to the renal veins are shown in Figure 1. The vertebral venous plexus and lumbar vein system take over its function. The vertebral venous plexuses (internal, see Fig. 2, and external) extend from the sacral region to the foramen magnum and make it possible for the circulation of blood to be initiated in the craniocaudal and caudocranial directions, or simply upward or downward, according to conditions of local pressure. In the pelvis, the vertebral plexus is connected to the inferior vena cava by the lateral sacral veins which join the hypogastric or common iliac veins and the middle sacral vein which joins the left common iliac vein.

In the lumbar area, the vertebral venous plexuses are connected to the inferior vena cava by the intervertebral veins to the lumbar veins (Fig. 3) which empty into the inferior vena cava as well as to the ascending lumbar veins which continue to the azygos and hemiazygos veins.

The lumbar portion of the iliolumbar vein (Fig. 3) inferiorly joins the hypogastric or common iliac vein, and superiorly continues to become the lumbar ascending vein, as mentioned previously, as it proceeds toward the thorax and becomes the azygos on the right and hemiazygos vein on the left side, respectively. Seib described 21 different patterns of the azygos system in dissections of human adult cadavers. This system has no valves; circulation can proceed inferiorly or superiorly and transversely in either direction to or away from the inferior vena cava according to the pressure relations existing at any moment. There is another demonstrable system, which has been called the renoazygolumbar canal. This system leaves the deep wall of the renal vein and inferiorly joins the ascending lumbar and superiorly joins the hemiazygos veins, respectively. Davis and associates have made an excellent review of the variations of lumbar, renal, and related venous communications from dissection of 100 specimens.

Other collateral pathways are available to carry blood from the pelvic area to the level of the upper part of the abdominal inferior vein. The venous plexus (Fig. 4), from

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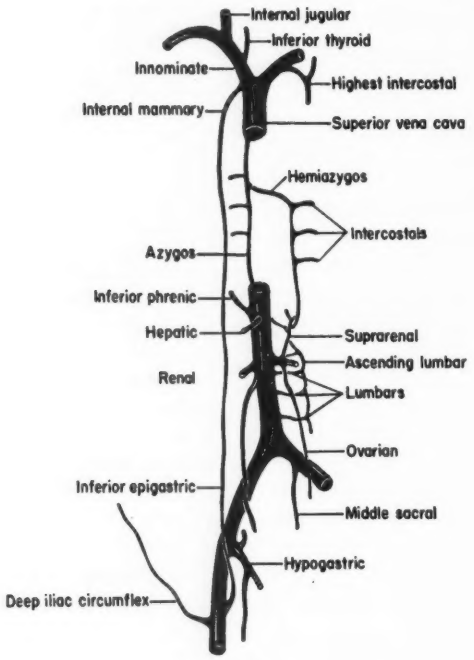

FIG. 1.

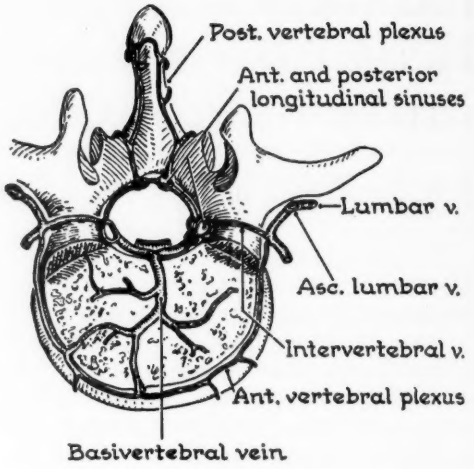

FIG. 2.

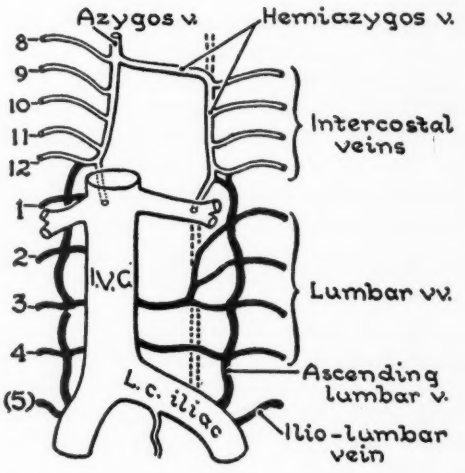

FIG. 3.

FIG. 1. Main branches and cross-connection of the superior and inferior vena cava. The chief branches of the venous tree. Parallel with the main inferior vena cava-superior vena cava stem, four additional pathways extend along the long axis of the trunk. These are the epigastric-mammary, the thoracoepigastric, the lumbar-hemiazygosazygos, and the internal vertebral systems. The second and the fourth indicated systems are not shown in the diagram. By permission of Quiring, D. P., Collateral Circulation, Lea & Febiger, Philadelphia (5).

FIG. 2. Vertebral venous system and connection with the lumbar veins. By permission of Grant, J. C. B., *A Method of Anatomy*, The Williams & Wilkins Co., Baltimore (3).

FIG. 3. The ascending lumbar vein, its origin and connection. By permission of Grant, J. C. B., *A Method of Anatomy*, The Williams & Wilkins Co., Baltimore (3).

the urethra, prostate, urinary bladder, uterus, vagina, and rectum intercommunicate with each other and join the right hypogastric and left hypogastric veins. These are also joined to the portal and external iliac veins. The spermatic or uteroovarian veins in the female drain the pampiniform plexus on the left to the left renal vein, and on the right to the inferior vena cava inferior to the right renal vein. These visceral anastomoses thus connect the area of drainage of the external iliac and hypogastric veins to the inferior vena cava and renal veins. The portal venous system (Figs. 5 and 6) is connected by anastomoses to the superior hemorrhoidal vein. Superiorly, it connects or anastomoses with the inferior mesenteric vein and inferiorly it connects or anastomoses with the middle hemorrhoidal vein by way of the hemorrhoidal plexus.

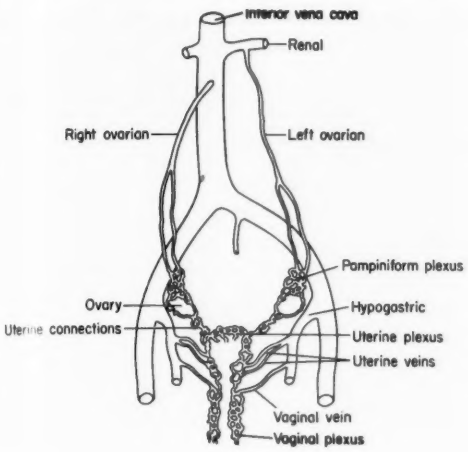

FIG. 4.

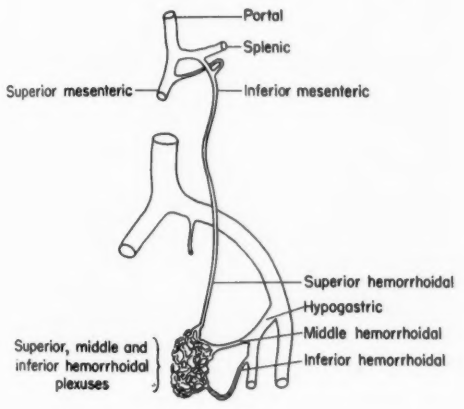

FIG. 5.

FIG. 4. Vaginal, uterine, ovarian collateral route. By permission of Quiring, D. P., *Collateral Circulation*, Lea & Febiger, Philadelphia (5). These venous channels parallel the arterial vessels to the same areas. Blood may be sent directly to ovarian veins from vaginal and uterine plexuses in case of obliteration of the hypogastric vein.

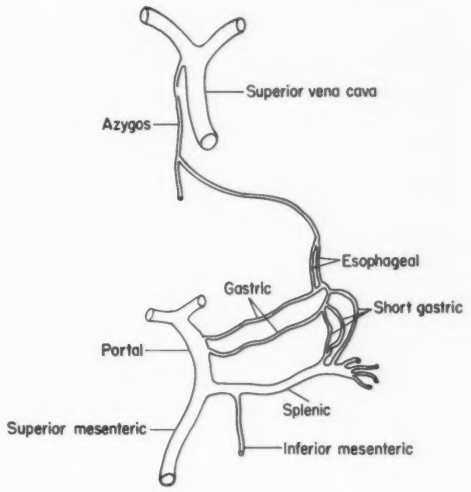

FIG. 6.

FIG. 5. Portal venous system, hemorrhoidal veins with associated plexuses. From Quiring, D. P., *Collateral Circulation*, Lea & Febiger, Philadelphia (5). Hemorrhoidal veins and associated plexuses. Closure of hypogastric vein permits blood to be carried via hemorrhoidal plexuses to superior hemorrhoidal vein which empties into inferior mesenteric. This offers direct communication between systemic and portal systems.

FIG. 6. Collateral channels from portal to systemic system. From Quiring, D. P., *Collateral Circulation*, Lea & Febiger, Philadelphia (5). Collateral channels from the portal to the systemic system. The gastric vein returns blood to the portal vein and also receives small esophageal veins which anastomose with the azygos vein which empties into the superior vena cava. The left gastric vein arises by union of small veins on both surfaces of the stomach. It runs along the lesser curvature to the esophagus, from which it receives tributaries. The esophageal veins are small and irregular. They drain the esophagus and form the connecting link whereby a part of the portal circulation may be deflected into the precaval vessel.

The middle hemorrhoidal vein joins the prostatic, seminal, and vaginal veins and these empty into the hypogastric vein. There is a connection with the inferior hemorrhoidal vein which empties into the internal pudendal vein. There are further anastomoses of minor importance that need not now be enumerated.

If the common and external iliac veins are occluded, there is an anastomotic connection around the ligation by way of the medial circumflex femoral vein and the obturator and inferior gluteal veins uniting the femoral vein by the channels to the internal iliac vein. If the femoral vein is occluded the internal saphenous vein and the spermatic or ovarian, as the case may be, is available as a pathway, using the channels of the external pudendal vein or the superficial dorsal veins of the penis; in each particular circum-

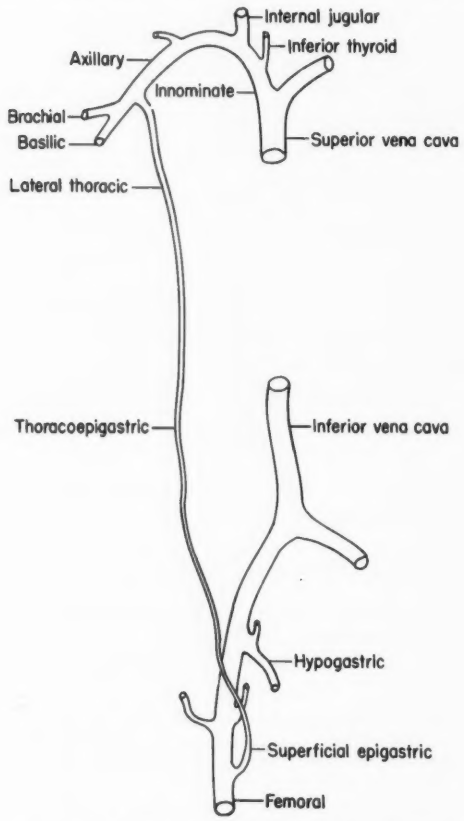

FIG. 7. The thoracoepigastric venous collateral pathway. From Quiring, D. P., *Collateral Circulation*, Lea & Febiger, Philadelphia (5). The thoracoepigastric venous collateral pathway. This channel affords a direct communication between the femoral and the axillary veins, permitting blood to bypass the entire inferior vena cava. In the event of occlusion of the subclavian vein, blood may pass from the basilic to the lateral thoracic and thence into the femoral vein.

stance, obstruction of the inferior third of the inferior vena cava ("low ligation") causes development or utilization of the superficial and deep veins of the abdominal wall on its anterior aspect. In the superficial pathway (Fig. 7), the latter veins are connections between the superficial circumflex iliac and superficial epigastric veins by means of the saphenous vein by using the upper lateral thoracic and abdominal veins to join the superior vena cava. The deep vein anastomosis consists of the deep circumflexiliac anastomosing with the superficial epigastric and lumbar veins connecting the external iliac veins with the ascending lumbar and internal mammary veins.

RATIONALE FOR INFERIOR VENA LIGATION

The flow of blood in a vein from the periphery, among other factors, is directly dependent on the resistance to flow in the vein. The pressure of blood already in the right atrium as well as the hydrostatic difference in the level or location of the vein in relationship to the heart influences the resistance to venous blood flow. Below a critical value, the diameter of a vein influences the resistance to blood flow. Any outside compression of a vein similarly alters the flow by affecting the size of the lumen of the vein. An example of this is abdominal ascites. The venous pressure on the extremities must rise above the pressure of the abdominal ascites before blood can reach the right atrium. Reduction of the lumen of veins by their own muscular action likewise affects the resistance to flow in them. The outflow of blood from the heart which is a measure of cardiac efficiency is dependent on the quantity of blood entering the right atrium. It is with this concept in mind that interest arises in the operative procedure of inferior vena cava ligation.

The concept is that tying the inferior vena cava lowers the strain that the overloaded right side of the heart places on a failing left ventricle by reducing the rate of venous return. The question is, At what level should this ligation be made to be most effective?

COMPARISON OF HIGH AND LOW LIGATION OF INFERIOR VENA CAVA IN DOGS

Studies have been made of inferior vena cava ligation and occlusion in male dogs weighing approximately 45 pounds each. Nembutal, 33 milligrams per kilogram, was used intraperitoneally for anesthesia. In some of the acute experiments, occlusion of the inferior vena cava and superior vena cava was maintained by passing Foley catheters down the external jugular vein and up the

FIG. 8.

FIG. 9.

FIG. 12.

FIG. 13.

FIG. 10.

FIG. 11.

FIG. 14.

FIG. 15.

FIG. 8. Demonstration of the renoazygolumbar canal.

FIG. 9. Occlusion of the superior vena cava and inferior vena cava, using a Foley catheter in each vessel. The former was passed through the femoral vein.

FIG. 10. Recent occlusion of the inferior vena cava near the bifurcation. The connections of the ascending lumbar vein and the inferior vena cava are seen. Comparison with Figure 11 shows almost a 4 to 5 fold compensatory enlargement of the azygos vein in the latter.

FIG. 11. Six months' occlusion of the inferior vena cava, of the dog of Figure 10, showing connections of the ascending lumbar vein and the inferior vena cava and compensatory enlargement of the azygos system.

FIG. 12. Recent occlusion of the inferior vena cava using a tie near the bifurcation. The collateral connections have taken over adequately immediately superior to the occlusion.

FIG. 13. Six months' occlusion corresponding to dog in Figure 12. The azygos system did not hypertrophy to any great degree, indicating that, in this instance, the collateral circulation has been adequate.

FIG. 14. Recent occlusion of inferior vena cava. The inferior epigastric, superior epigastric, and internal mammary veins are demonstrated.

FIG. 15. Six months' occlusion of inferior vena cava of dog in Figure 14. The superficial collateral abdominal circulation is not demonstrable in this instance. The azygos system is much larger than in Figure 16.

femoral vein. At various levels it was possible to inflate the small rubber balloon at the end of the catheter and so occlude the vessel. Following this procedure, an injection of opaque medium into the femoral and external jugular veins was made. The opacification of the vertebral, renoazygos lumbar, azygos, and caval system was studied.

FIG. 16.

FIG. 17.

FIG. 16. Recent occlusion of the inferior vena cava near the renal veins. The superficial collateral circulation on the abdominal wall is outlined. The ascending lumbar and azygos system has not shown compensatory hypertrophy at this point.

FIG. 17. Six months' occlusion of the inferior vena cava in renal area of the dog shown in Figure 16. This marked hypertrophy of the ascending lumbar vein and the azygos vein. The inferior epigastric, superior epigastric and internal mammary are not demarcated as in Figure 16.

Reproductions of some of the roentgenograms appear with this article (Figs. 8 and 9). The dog could maintain life with occlusion of the superior vena cava above the entrance of the azygos and occlusion of the inferior vena below the renal veins for well over a 2½ hour period (Fig. 9).

Andreasen and Watson, surgically occluded both cavae for 30 minute periods. They stated this was accompanied by a five fold increase in azygos blood flow. Other collateral pathways designated in the preceding anatomic description were clearly outlined according to the level of venous occlusion, including the inferior epigastric, superior epigastric, and internal mammary vein anastomoses (Fig. 7).

Chronic experiments were performed on 6 healthy male dogs. Roentgenograms of these results are shown for comparison with the effects of acute ligation (see Figs. 10 and 11, 12 and 13, 14 and 15, 16 and 17). The pictures were taken approximately 6 months apart. All operations were performed in January 1959. In 3 of the dogs (Figs. 10 to 15) the ligation was placed near the bifurcation of the inferior vena cava. In the other 3 dogs (Figs. 16 to 20) the ligation was placed immediately below the renal veins. A renal approach was made from the right side and the inferior vena cava vein tied with heavy silk. The operative procedure is not difficult; the length of operating time from the primary incision to closure did not exceed 30 minutes. The inferior vena cava with its branches is quite friable; reasonable care has to be used in this regard. Angiographic studies of these dogs were made in January and in July 1959. These dogs were in excellent physical condition at all times, although confined to individual cages.

There was a moderate dilatation of the superficial veins on the anterior abdominal wall. Radiologic comparisons of the acute and chronic states indicate the following:

1. In tying the inferior vena cava near the bifurcation, there is a marked possibility that in a short time the inferior vena cava will function just superior to the ligation. This is the result of the lumbar veins in the area, which have good anastomotic connections with the vessels immediately below and above the ligature. This function takes over within minutes after ligation. Ligation at this level acts like a "detour," the same highway carrying most of the traffic immediately beyond it. The report of Davis and associates would substantiate this finding in man.

2. The anastomotic collateral return just described is somewhat variable, since sometimes at this level anastomotic collateral return to the right side of the heart very occasionally is similar to that of a ligation made near the renal vein.

3. The superficial collateral return by way of the inferior epigastric, superior epigastric, and internal mammary veins is more pronounced immediately after ligation. It tends to lessen in size as the deeper collateral pathways become more adequate.

4. There is marked hypertrophy of the azygos vein system in 6 months when inferior vena cava ligation is near renal veins.

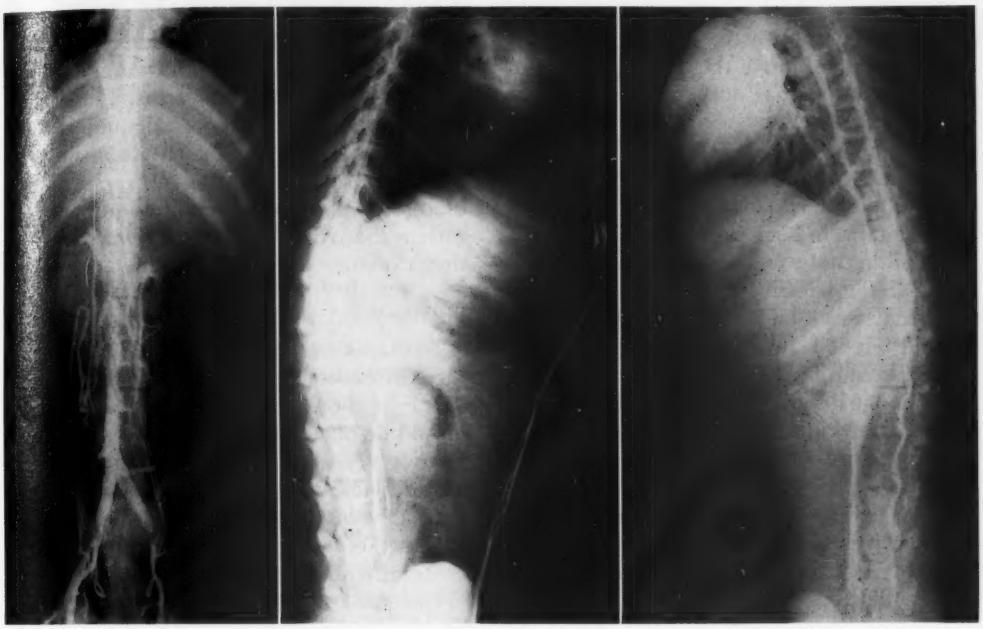

FIG. 18. FIG. 19. FIG. 20.

FIG. 18. Occlusion of the inferior vein, 6 months postoperatively, which shows development and compensatory hypertrophy or renoazygolumbar venous systems.

FIG. 19. Recent occlusion near the renal veins of the inferior vena cava which demonstrates the superficial collateral circulation on the anterior abdominal wall.

FIG. 20. Six months' postoperative ligation of inferior vena cava near renal vein (Fig. 19). There is compensatory hypertrophy of ascending lumbar and azygos veins. The superficial abdominal veins are not shown.

5. The enlargement of the azygos vein in the lower venous ligations near the bifurcation of the inferior vena cava is less if the lumbar veins are adequate in returning blood to the inferior vena cava just above the tie.

These findings show that when ligation is made near the bifurcation of the inferior vena cava, the inferior vena cava may rapidly become patent just above the tie resulting from the adequate collateral return from the lumbar veins, some quite large.

If the tie is near the renal veins of the inferior vena cava, the blood from below the level returns by way of the azygos vein to the superior vena cava. The hypertrophy of the azygos vein confirms this observation.

Clinical ligation of the inferior vena cava is almost always performed without regard for differences between low and high ties. This fact probably accounts for the varied opinions of the merit of caval ligation.

DISCUSSION

In reference to the results of the experiments with dogs, it was suggested that the optimum area of ligation to reduce inferior vena caval flow is just below the renal veins. This is so since ligation low down may serve as no real barrier to venous return by way of the inferior vena cava. It should be noted that the better results in the operation for relief of advanced cardiac failure have been in those cases in which collateral circulation was not readily established, such as would be the situation if the ligation were done near the bifurcation of the inferior cava. In this area there is an abundant collateral return to the inferior vena cava by way of the lumbar veins and their connections. The azygos route return plays a predominant role in the return of blood to the right atrium when the ligation is near the renal veins. This was demonstrated in this study

both acutely and by the hypertrophy of the azygos after 6 months.

Karaev mentioned the improvement of kidney function that occurred in his work. This is explained by the improvement of cardiac function and resultant hemodynamics. On speculation, the improvement of kidney function could result from the lowering of renal vein back pressure, based on the assumption that a rise of renal vein pressure, caused by congestive failure, results in an abnormal production of renin, similar to that developed in dogs by experimental compression bilaterally of the renal arteries. This change in renal function could be quite different in origin from that caused by the back pressure of congestive failure. The possibility also exists that both factors act together to depress kidney function. The resultant disturbance of electrolyte balance obviously aggravates congestive failure to a marked degree.

It would appear that ligation of the inferior vena cava at the renal level acts in two ways; there is lessening of the strain on the right side of the heart, with improvement of water balance; there is an increase of kidney function with improvement of electrolyte balance.

Inferior vena caval ligation should be reserved for patients with thromboembolism who do not respond to medical treatment. It should also be reserved for patients with recurring multiple emboli who do not respond to anticoagulant therapy. The optimum position, other things being equal, suggested by the results of these experiments in the dog would be immediately above the bifurcation of the inferior vena cava.

Inferior caval ligation may be used in operative treatment of advanced cardiac decompensation when ordinary measures of usual cardiac surgery are not applicable. The operation might be compared to a palliative procedure similar to gastroenterostomy for inoperable carcinoma However, the results should be much better if the myocardial changes have not become so progressive that they are irreversible.

If the operation of ligation is performed to relieve cardiac insufficiency the experimental results suggest that the optimum level of ligation is near the renal veins. The azygos vein functions much more adequately, and the hemodynamics of the situation suggests that this is so. The lumbar veins return their blood by way of the ascending lumbar veins rather than by the inferior vena cava as they do when the ligation is low.

SUMMARY

In those cases of pulmonary embolism and thromboembolism in which inferior vena caval ligation is applicable, the ligature should be placed near the bifurcation of the inferior vena cava. This method allows for an adequate and early functioning of the lumbar veins which are able in many cases to return blood to the inferior vena cava immediately above the tie.

In those cases of cardiac failure in which ligation of the inferior vena cava is contemplated, the tie should be placed near the renal veins. There is much greater utilization of the azygos return at this level. The lumbar veins return blood in this situation by way of the ascending lumbar veins which join the azygos system. This could act in two ways: (1) by reducing somewhat the strain on the right side of the heart, and (2) improved kidney function by reduction of back pressure in the inferior vena cava. The former helps to correct the fluid disturbances, the latter the electrolyte imbalance.

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SURGICAL CORRECTION OF AORTIC INSUFFICIENCY ASSOCIATED WITH VENTRICULAR SEPTAL DEFECT

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THE ASSOCIATION of aortic insufficiency and ventricular septal defect imposes difficult problems in preoperative diagnosis and surgical correction. Though the autopsy finding of this combination of lesions has been reported, precise diagnosis by contrast visualization followed by corrective operation has not hitherto been noted in the literature.

The incidence of aortic insufficiency with ventricular septal defect is difficult to ascertain, since a clinical diagnosis may be open to question. Scott and associates (6) collected 22 autopsy cases and Denton and Pappas reported 1 additional autopsy case. Thus, 23 well documented cases are available for review with particular reference to the location of the ventricular septal defect and aortic valve insufficiency. In all cases, the ventricular septal defect was described as high in the septum or in the membranous septum. The defect was located immediately beneath the right coronary cusp in 13 cases, the posterior, noncoronary cusp in 2 cases, both the right coronary and posterior cusp in 1 case, and not designated with relationship to a specific cusp in 7 cases. In 9 cases, the right coronary cusp of the aortic valve was noted to prolapse downward into the left ventricle and ventricular septal defect. In 3 cases the posterior cusp was involved in this manner, and in 1 case both right and posterior cusps were prolapsed. In 1 case, the aortic valve was noted to be prolapsed but the cusp was not specified. In 2 instances, the valve cusp overriding the ventricular septal defect was found to be fenestrated, and in 1 a fissure in the right cusp was described. In the remaining 6 cases, the mechanism by which regurgitation occurred was not noted.

Clinically, this lesion is characterized by a to-and-fro murmur along the left sternal border and a wide arterial pulse pressure. The chest roentgenogram usually shows cardiac enlargement and the increased pulmonary markings of left to right shunting. The electrocardiogram may show left ventricular hypertrophy. The differential diagnosis involves patent ductus arteriosus with or without ventricular septal defect, aorticopulmonary septal defect, coronary arteriovenous fistula, and ruptured aneurysm of the sinus of Valsalva. Ledbetter and associates have been the first to diagnose ventricular septal defect and aortic insufficiency during life by means of dye dilution techniques. The use of angiocardiographic techniques for diagnostic examination of the left side of the heart has not been described in previous reports.

CASE REPORTS

CASE 1. K. F., an 8 year old white female, was admitted to the Doernbecher Unit of the University of Oregon Medical School Hospital on 16 January 1959 for a cardiac operation. She was known to have had a murmur since birth, and growth and development were normal. She had frequent respiratory infections in early childhood but no exercise limitation. At the time of the patient's first catheterization of the right side of the heart at the age of 4 years, confirming the clinical diagnosis of ventricular septal defect (Table I), a grade 4 to 5 pansystolic murmur was present over the precordium. There were no diastolic murmurs noted, and arterial blood pressure was 104/58 millimeters of mercury. A chest roentgenogram re-

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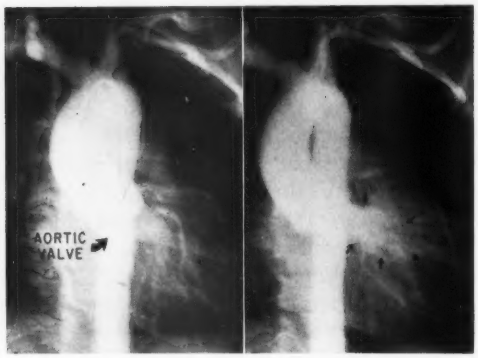

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FIG. 1. Case 2. Injection made into the supravalvular proximal thoracic aorta. a, Late systole. Arrow indicates level of aortic valve. Aortic regurgitation is present but shows to considerably better advantage on the film exposed during the succeeding diastolic phase. b, Diastole. A clearly defined regurgitant jet of opaque substance has traversed the aortic valve and is seen (arrows) within the left ventricular outflow tract.

vealed cardiac enlargement and increased pulmonary vascularity. An electrocardiogram showed the pattern of an incomplete right bundle branch block and remained unchanged during follow-up. In May 1956, a decrescendo diastolic murmur was noted at the base, and a retrograde aortogram by way of the left brachial artery failed to disclose a patent ductus arteriosus. In October 1957, catheterization of the right side of the heart was unchanged from previous findings.

TABLE I.—CARDIAC CATHETERIZATION DATA FROM CASE I

Sample No.	*Position*	*Pressures, mm. Hg*	*O_2 content, vol. per cent*	*O_2 saturation, per cent*
Date of procedure: 8 July 1955*				
1	Rt. PA		13.04	82.6
		Mean: 10		
2	Main PA	16/5		
3	RV	24/4	11.76	74.5
4	LV	110/22		
5	RA		11.91	75.4
6	SVC		11.19	70.9
7	Lt. FA		15.16	96.0
Date of procedure: 4 October 1957†				
	LV	128/8		
1	Rt. PA	22/12	13.25	76.5
	Main PA	24/10		
2	PA just above valve		14.31	82.7
3	RV just below valve		14.05	81.2
4	RA		11.43	66.0
	Hi RV	33/6		
	Mid RV	44/7		
5	SVC		11.54	66.7
6	Rt. FA		16.48	95.2

*O_2 capacity: 15.79 vol. per cent.
†O_2 capacity: 17.31 vol. per cent.

On the patient's admission to the hospital prior to operation, physical findings were unchanged, and operation was performed on 21 January 1959. The heart was approached through a midline sternum-splitting incision, and upon opening the pericardium it was found that the left ventricle appeared moderately enlarged. A systolic thrill was palpated over the right ventricular outflow tract and proximal pulmonary artery and a diastolic thrill could be palpated over the pulmonary artery and proximal aorta. Neither patent ductus arteriosus nor aorticopulmonary septal defect was present. A ruptured aneurysm of the sinus of Valsalva was not palpated through the right atrial appendage. The patient was placed on cardiopulmonary bypass using a rotating disc oxygenator and rotary pumps at a flow of 2.6 liters per square meter of body surface per minute. A satisfactory perfusion was immediately apparent and a catheter was placed in the left ventricle for decompression should residual aortic insufficiency be present after cardiac arrest. When the right ventricle was opened a ventricular septal defect was found approximately 1 centimeter in diameter and lying in the region of the crista supraventricularis through which the right and posterior cusps of the aortic valve were seen to prolapse. Because of aortic regurgitation the proximal aorta was cross-clamped and the heart was arrested with potassium citrate. The defect was closed with interrupted no. 4-0 silk sutures and after 7 minutes of cardiac arrest the aortic clamp was removed. Despite left ventricular catheter decompression, massive distention of the left ventricle occurred and perfusion pressure fell to 0. The aorta was reclamped to allow the heart to decrease in size. The clamp was removed a second time while the aortic valve was supported by digital pressure against the root of the aorta. Sinus rhythm returned and the ventricular septal defect closure was inspected and found to be bloodtight. The ventriculotomy was closed and the patient was taken off bypass after a total perfusion time of 50 minutes. After closure of the thoracotomy a tracheostomy was performed. The patient was returned to the recovery room with a normal arterial and venous pressure but requiring ventilatory assistance. She responded to painful stimuli but never regained consciousness. The pulse was abrupt, and a loud grade 3 diastolic murmur of aortic insufficiency was present. Hypotension unrelated to blood loss developed on the evening of the operative day and, despite intravenous administration of digitalis, the patient died 10 hours after operation.

Autopsy revealed marked pulmonary congestion. The brain appeared normal. The heart weighed 180 grams. The left ventricular wall was 10 to 12 millimeters in thickness, and the right ventricular wall was 3 millimeters in thickness. The right and posterior aortic cusps were thickened, and the free edges were elongated. The suturing of the ventricular septal

defect did not prevent prolapse of these cusps into the left ventricle. The ventricular septal defect was lying immediately below the right and posterior cusps high in the septum and was 1 centimeter in diameter. One of the sutures had pulled out of the margin of the defect.

CASE 2. B. K., a 9 year old white female, was admitted to the Doernbecher Unit of the University of Oregon Medical School Hospital on 21 October 1959 for a cardiac operation. At the age of 2 weeks a heart murmur was noted and at 7 months of age pneumonia developed with cardiac failure for which the patient was digitalized. Frequent respiratory infections continued, and in October 1954 cardiac catheterization was performed and revealed a left to right shunt at the ventricular level as noted in Table II. Physical examination at that time revealed abnormalities related only to the cardiovascular system. The patient's blood pressure was 110/44 millimeters of mercury and the heart was enlarged to percussion. A systolic thrill was palpable over the third and fourth intercostal spaces to the left of the sternum and a grade 4 to 5 pansystolic murmur was audible over the entire precordium. No diastolic murmurs were heard. However, in May 1958 a diastolic murmur was heard for the first time, and cardiac catheterization repeated on 9 May 1958 again revealed a ventricular septal defect (Table II). Physical examination prior to operation revealed a systolic murmur as before and a grade 2 to 3 blowing early diastolic murmur at the base transmitted downward toward the apex. Blood pressure was 130/40 millimeters of mercury and an electrocardiogram revealed borderline left ventricular hypertrophy. An angiocardiogram of the left side of the heart (Figs. 1 and 2) demonstrated a ventricular septal defect and aortic insufficiency(3).

Operation was performed on 28 October 1959 through a median sternotomy incision. The left ventricle was found to be enlarged and the pulmonary artery was larger than the aorta. A systolic thrill was palpable over the right ventricle and proximal pulmonary artery and no diastolic thrills were present. Cardiopulmonary bypass was instituted by using the rotating disc oxygenator and rotary pumps at a flow of 2.9 liters per square meter of body surface per minute, and at this time a diastolic thrill was easily palpable over the aortic valve. As soon as a satisfactory bypass was evident the patient was cooled to 30 degrees C. A catheter was introduced into the left ventricle and 10 minutes after the onset of perfusion the aorta was cross-clamped and the right ventricular outflow tract was opened. Perfusion of the pericardium with saline cooled to 4 degrees C. was started and continued until coronary flow was resumed. A ventricular septal defect 7 millimeters in diameter with a fibrous margin was found lying on the crista supraventricularis. Intermittent release of the aortic clamp revealed marked regurgitation from the aorta through

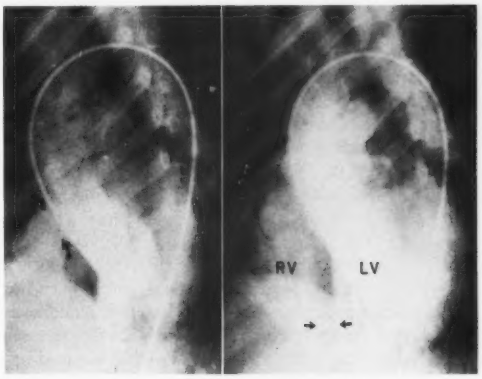

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FIG. 2. Case 2. Injection into the left ventricular cavity. Films exposed in right posterior oblique projection. a, A film exposed during systole shows (between arrows) a jet of opaque substance traversing the upper anterior portion of the ventricular septum to enter the right ventricular cavity. b, The succeeding diastolic view shows the relative size of both ventricular cavities to better advantage. Small arrows bracket the opaque shadow of the interventricular septum. Such studies provide positive diagnostic and valuable anatomic information in ordinary ventricular septal defects as well as in those associated with aortic insufficiency.

the defect. The ventricular septal defect was closed with interrupted No. 3-0 silk sutures and the aortic clamp was removed after 4 minutes of occlusion. After 4 minutes of coronary perfusion the aorta was again cross-clamped for 22 minutes during which time it was opened and the regurgitation was cor-

TABLE II.—CARDIAC CATHETERIZATION DATA FROM CASE 2

Sample No.	*Position*	*Pressures, mm. Hg*	*O_2 content, vol. per cent*	*O_2 saturation, per cent*
Date of catheterization: 18 October 1954*				
1	PA	16/8 Mean: 7	12.62	86.0
2	PA	13/5		
3	RV (High)	42/4 Mean: 0	12.56	85.6
4	RA	2.6/1.3	11.22	76.5
5	SVC		11.05	75.3
Date of catheterization: 9 May 1958				
1	Rt. PA		12.56	80.6
	Main PA	38/13		
	Main RV	47/8		
2	RA	4 mm. Hg	11.19	72
3	RA		11.32	73
4	RV Infund.	41/8	12.36	79
5	IVC (just below diaphragm)		12.07	79
6	SVC		11.26	72.27
7	Lt. FA		15.27	98.01

*O_2 capacity: 14.67 vol. per cent.

rected. The aortic valve was bicuspid as shown in Figure 3. There was a right and left cusp with the line of closure running in an anterior to posterior direction. The right cusp was thickened and elongated along its free edge and hence could prolapse below the left, causing insufficiency.

The method of correction was as shown in Figure 3. One suture of No. 3-0 silk was placed through the thickened free edge of the right cusp near the posterior commissure and then through the aortic wall at the level of the posterior commissure. A second suture was placed through the free edge of the right cusp anterior to the first and then through the left cusp at the posterior commissure. When these were tied over a pledget of compressed ivalon sponge the free margin of the right cusp was shortened, allowing approximation of the bicuspid valve in the same plane. The aortotomy was closed with No. 3-0 silk and the patient was rewarmed. Upon removal of the aortic clamp ventricular fibrillation developed but left ventricular distention did not occur. Electric defibrillation resulted in a sinus rhythm after the first shock. The ventriculotomy was closed and the left ventricular catheter was removed, care being taken to remove all air from the chamber. The patient was taken off bypass without incident after a total perfusion period of 62 minutes. She was returned to the recovery room with a normal arterial and venous pressure and weighing 100 grams heavier than her preoperative weight. Transient hypotension on the afternoon of operation responded to vasopressors and blood replacement. During the first postoperative week, signs of mild congestive failure were apparent but responded well to increased digitalis. Ambulation was started during the second postoperative week and the patient was discharged during the fourth postoperative week with an arterial pressure of 100/70 millimeters of mercury. Systolic thrill was absent from the precordium and a grade 1 systolic ejection murmur was audible over the left third intercostal space. No diastolic murmurs were present.

DISCUSSION

Although the association of aortic insufficiency with ventricular septal defect is uncommon, the 2 patients presented in this report were among a group of 28 with isolated ventricular septal defects operated upon in a series of 100 open heart surgical procedures at the University of Oregon Medical School Hospital. Of paramount importance in a successful surgical attack is a correct preoperative appraisal of the presence and pathogenesis of aortic insufficiency. The catastrophic effect of unrecognized aortic insufficiency at the time of open heart surgery, especially when elective asystole is used as an adjunct, has been well documented by Clauss, Baker, and Altemeier. These include the loss of perfusate into the operative field with resultant drop in perfusion pressure, distention and subsequent damage to the left ventricle, and pulmonary capillary damage resulting from distention of the pulmonary venous circulation. The loss of the patient in Case 1 was undoubtedly related to one or more of these factors.

It is of interest that in both patients the diastolic murmur of aortic insufficiency was not present on initial examination but developed during the course of observation prior to operation. This may be an important differential diagnostic feature of this combination of defects. The blowing immediate diastolic murmur of aortic insufficiency must not be confused with the rumbling apical diastolic murmur of increased mitral flow associated with ventricular septal defect.

Roentgenographic studies with injection of contrast material above and below the aortic valve through a spring guided catheter passed into the aorta through the brachial or femoral artery allow precise diagnosis through visualization of the ventricular septal defect and of the aortic regurgitant jet. Prior to operation examination by this technique is performed in the Department of Radiology at the University of Oregon Medical School upon all patients with suspected aortic valvular disease.

The mechanism resulting in aortic insufficiency has been well documented in autopsy material, and in the majority of instances there is prolapse of the right or posterior cusp or of both right and posterior cusps into the left ventricular outflow tract immediately above or through the ventricular septal defect. In the first patient in this report both right and posterior cusps were prolapsed through the ventricular septal defect and easily visible at the time of ventriculotomy. In the second, the right cusp of a biscuspid aortic valve was prolapsed

downward but did not present in the ventricular septal defect itself. The occurrence of the diastolic murmur in both cases late in the course of observation suggests that the prolapse is not congenital but is in some way secondary to the ventricular septal defect. Perhaps the high velocity jet of blood passing through the ventricular septal defect pulls the aortic leaflet downward. If this is so, one wonders why ventricular septal defects in this location are not associated with aortic insufficiency more often. In addition, correction of the ventricular septal defect alone in Case 1 did not, as was hoped, alleviate the aortic insufficiency. At autopsy on this patient it was apparent that closure of the ventricular septal defect in any direction did not allow sufficient support of the right and posterior cusps.

Surgical correction, therefore, should be directed toward the aortic valve as well as the ventricular septal defect. If the mechanism of aortic insufficiency be leaflet prolapse, this prolapse must be associated with elongation of the free edge of the leaflet. Shortening the free edge of the involved leaflet in a manner similar to that shown in Figure 3 is indicated. Fortunately, the free edge of the prolapsed cusp is thickened, possibly as the result of turbulent blood flow, and appears to hold sutures well. This thickening has been noted in most of the autopsy reports found in the literature. If the mechanism of aortic insufficiency be fenestration of a cusp, this lesion may be corrected by direct suture, if the margins are fibrous, as described by Scott and associates (5), or by the employment of an onlay graft of pericardium or synthetic material. After repair of the valvular lesion, residual aortic insufficiency may lead to massive left ventricular distention on removal of the aortic clamp. For this reason, if a beating heart is not maintained by coronary artery perfusion, a catheter should be placed in the left ventricle. Although this may not be adequate in decompressing the left side of the heart in the presence of massive aortic insufficiency, it is of value

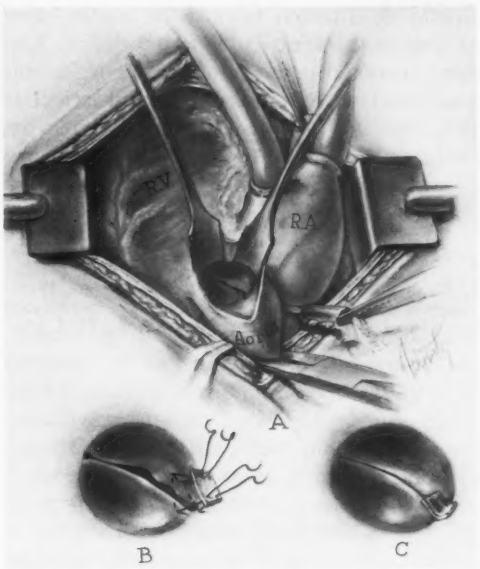

FIG. 3. The aortic valvular lesion at the time of aortotomy is shown to consist of a bicuspid valve with prolapse of the right cusp. The free edge of this cusp is thickened and elongated. A method of correction is shown in insets.

if aortic run-off is small. Should ventricular fibrillation occur, some means of insuring against distention of the left ventricle or the left atrium is mandatory. Decompression by the left ventricular route has the additional advantage of enabling removal of trapped air and is used routinely in this clinic in all operations upon the aortic and mitral valves for which the patient is in a supine position.

SUMMARY

Surgical experience with 2 patients with aortic insufficiency and ventricular septal defect in a series of 100 open heart operations, including 28 isolated ventricular septal defects, is presented. The delayed occurrence of the murmur of aortic insufficiency may be an important differential diagnostic sign from other conditions that may mimic this combination of lesions. Accurate anatomic diagnosis can be made preoperatively by techniques for visualization of the left side of the heart, and surgical therapy

should be directed toward the aortic valve as well as the ventricular septal defect. The most common cause of aortic regurgitation associated with ventricular septal defect is prolapse of the right or posterior cusp or both, and a method to correct this prolapse by suturing the free edge of the involved leaflets is described.

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AN EXPERIMENTAL STUDY OF THE ROLE OF HEPATIC LYMPH IN THE PRODUCTION OF ASCITES

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MANY FACTORS have been incriminated as the sole or a contributing cause of ascites, whether it be due to hepatic disease, cardiac disease, or venous obstruction between the liver and the heart. These factors include portal hypertension, hypoalbuminemia, renal retention of sodium and water, hormonal alterations, and increased capillary fragility. Recently, a number of investigators have indicated that the primary factor in the causation of this transudate is the extrusion of hepatic lymph secondary to postsinusoidal hepatic obstruction with hepatic congestion. Many bits of evidence lend support to this thesis.

After injecting colored plastics into the three major vessels, Madden and his associates studied the vascular supply of the human liver at autopsy and showed quite clearly that constriction with obstruction in the hepatic venous system was the *sine qua non* of ascites formation. On the basis of these studies they recommended that hepatopexy be utilized in the treatment of this problem. The results, however, have not been very rewarding. Baggenstoss and Cain studied the number and size of hepatic lymphatics in the transected porta hepatis of patients with ascites from various causes and found that there was a distinct increase in number and size of these lymphatic channels in the patients producing ascites. After cannulating the main hepatic efferent lymph channel, Cain and his coworkers showed—in the dog with inferior vena cava constriction and active ascites production—a markedly increased flow of hepatic lymph. Although this increase in flow suggests hepatic congestion, it does not necessarily implicate extrusion of hepatic lymph through Glisson's capsule into the peritoneal cavity as a causative factor in ascites. Freeman indicated that he and Ivy had placed the liver of the dog into the chest after thoracic inferior vena cava constriction and noted that in these animals fluid was accumulated in the thorax but none or virtually none within the abdomen. They did not describe the technique of the procedure nor did they present objective data. Mallet-Guy and his associates attempted the same experiment but were unsuccessful in translocating the whole liver; they then moved only one or several lobes of the liver into the chest and, after partial hepatic vein constriction of the respective lobe or lobes, found pronounced hydrothorax formation within several weeks in each animal. This specific localization of the fluid to the chest with an absence of fluid from the abdomen would very strongly indicate that the source of this fluid, in the animal preparation used, is extrusion of lymph from the surface of the liver. Hyatt, Lawrence, and Smith, observing dogs with thoracic inferior vena cava constriction, wrapped a plastic bag about the swollen, congested liver and found that fluid could be collected rapidly and easily in this bag. They were also able to observe droplets of fluid collecting and falling from the liver surface. More recently, Gage and his collaborators, on the basis of this and other information, advocated hepatopexy in the correction of this complication. He and his coworkers were able to prevent the accumula-

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TABLE I.—FLUID ACCUMULATIONS IN ANIMALS AFTER THE TWO STAGE OPERATION

Animal No.	*Hydrothorax, c.c.*	*Ascites, c.c.*	*Intrapleural adhesions*
471	500	30	+++
1056	800	0	+++
1120	650	100	+++

TABLE II.—FLUID ACCUMULATIONS IN ANIMALS AFTER THE ONE STAGE OPERATION

Animal No.	*Hydrothorax, c.c.*	*Ascites, c.c.*	*Intrapleural adhesions*
	GROUP 1		
283	550	60	++
211	720	250	++
1216	700	0	+++
238	900	160	+++
850	500	0	+++
697	325	75	+++
785	700	100	+++
507*	800	425	++
	GROUP 2		
246	350	350	++
253†	700	780	None
346	400	400	+++
851	250	300	++++
207	570	450	+++
	GROUP 3		
214†	100	0	++++
1081	0	0	+++
7	0	0	++++
49§	200	0	+
604	200	0	++++
277§	0	0	++++
220‡	300	1100	++++

*Pleural and peritoneal cavities communicated through a rent in the diaphragm along the inferior vena cava.
†Free pleuroperitoneal communication on the left.
‡One lobe projected into the lesser peritoneal sac.
§Only minimal constriction of the thoracic inferior vena cava.

tion of ascites after vena cava constriction in the dog by completely obliterating the peritoneal surfaces of the liver by trauma and talcum poudrage.

All of this evidence implicates extrusion of fluid from the surface of the liver as the major if not the sole cause of ascitic fluid in the experimental animal and presumably, therefore, in the cirrhotic patient with ascites. The experiment of Freeman and Ivy seemed critical and clear cut and warranted documentation. Therefore, an endeavor was made to place the entire liver within the chest of dogs and then to constrict the inferior vena cava within the chest.

METHOD

Healthy mongrel dogs were used. The method for the translocation of the liver into the chest has been previously reported (3). At the present time a one stage procedure is performed exclusively in which the liver is placed completely within the chest, the diaphragm is repaired beneath it, and the thoracic inferior vena cava is wrapped snugly with a strip of reactive polyethylene. Within 2 or 3 weeks the vena cava is properly constricted and fluid accumulation occurs. A few factors about the technique warrant emphasis: (1) The anesthesia must be perfect, with strict avoidance of barbiturates; (2) the left phrenic nerve must be preserved; (3) the animal must be given whole blood during the operative procedure; and (4) antibiotics in large doses must be given before, during, and after the operative procedure.

The present mortality rate with the operative procedure approaches 50 per cent, but during the early phases of the experiment it was closer to 90 per cent. Most of the deaths occur during or soon after the operation and appear to be related to disordered cardiac function. Postoperative care consisted of diet as tolerated, antibiotics, unlimited activity, and parenteral alimentation when indicated. All animals were observed carefully till death or were sacrificed 3 to 4 weeks after the operative procedure. All animals were autopsied and the volumes of clear fluid within the chest and abdomen were noted and recorded. The total volume of fluid within the two pleural cavities was added in order to obtain the volume of hydrothorax.

RESULTS

Twenty-three animals survived the operative procedure for a long enough period to be considered in the analyses. Three of these animals were operated on by the original, two stage method; that is, the liver was placed within the chest, and at a subsequent operation the vena cava was constricted to 50 per cent of its original diameter. The fluid accumulations in these 3 animals are indicated in Table I. The striking finding in each animal was the large volume of hydrothorax and the small volume of ascites.

Because of the high mortality of the second operation in animals with the liver in the chest, the operative procedure was modified so that the liver translocation and the caval constriction could be effected with a single operation. Twenty animals survived the present, one stage operation long enough to be considered in the analyses. The significant data concerning the fluid accumulations at autopsy in these animals are shown in Table II. The animals were arbitrarily placed in 1 of the 3 groups according to the relative volumes of fluid within the chest and abdomen. In group 1 are listed the animals with significantly greater volumes of fluid within the chest than within the abdomen. In group 2 are listed the animals in which the volumes of fluid in the two spaces are approximately the same. Animal No. 253 of this group had a definite, mesothelium-lined communication between the left pleural cavity and the peritoneal cavity so that fluid could probably move from one cavity to another. The total volume of pleural and peritoneal fluid in this animal was considerably greater than in the others of the group and there were very few adhesions between the liver and the surrounding viscera in this animal. However, in all other animals of this group, adhesions between the liver and surrounding structures were present to a moderate or marked degree. In group 3 are listed the animals with a satisfactory preparation in which there was minimal accumulation of fluid in the mesothelial cavities. There was question about the degree of constriction of the vena cava in animals Nos. 49 and 277; this might explain the absence of fluid. In the other 4 animals, however, the constriction of the vena cava was definite and yet the fluid accumulation in the mesothelial cavities was minimal. Animal No. 214 was found to have a mesothelium-lined communication between the left pleural cavity and the peritoneal cavity. There was very marked adhesion formation between the liver and surrounding intrathoracic structures in animals Nos. 214, 7, and 604.

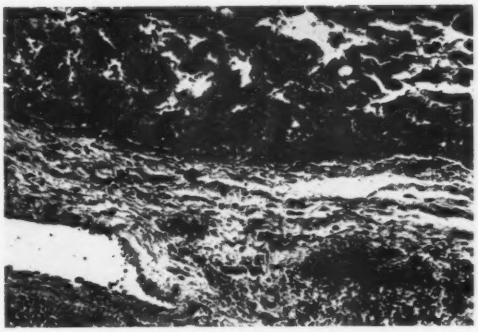

FIG. 1. Section of liver and overlying adhesion to lung. No lung tissue is shown. Note the large vascular channels at lower left. The cleft-like spaces in the middle right are enlarged, subcapsular lymphatic spaces of the liver.

The microscopic pattern of all thoracic livers in dogs with definite vena cava constriction was one of severe congestion and minimal to moderate cellular destruction. There was no microscopic evidence of fibrosis. In Figure 1 are shown the large vascular channels—blood or lymph—in the fibrous adhesions between the liver and the lung. In Figure 2 are shown similar connections between the liver and the diaphragm. These are sections from animals in group 3 in which there was very little fluid in either the thoracic cavity or the peritoneal cavity.

DISCUSSION

In approximately half of these animals there was more fluid in the chest than in the abdomen at the time of death or sacrifice. In about one-fourth of the animals there were similar volumes of fluid in the two spaces, and in the other one-fourth there was minimal fluid in both cavities. In only 1 animal, No. 220, was there more fluid within the abdomen than within the chest. In this animal there was a very significant finding at autopsy to explain this fluid distribution: one of the lobes of the liver had dropped through a defect in the diaphragm to lodge within the lesser peritoneal sac. It was well walled off from the pleural cavities, but was not at all walled off from the structures within the lesser peritoneal sac. This animal represents to us the reverse

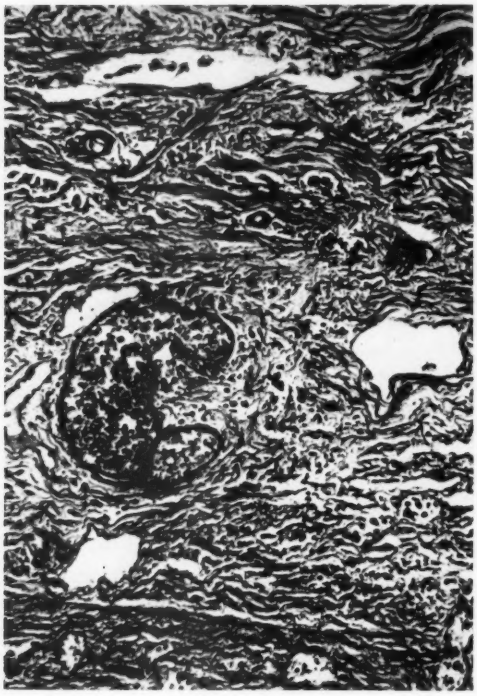

FIG. 2. Multiple vascular channels present in a dense adhesion between liver and diaphragm. Liver is inferior and diaphragm superior to the field shown.

of the Mallet-Guy experiment. The large volume of fluid within the peritoneal cavity was the result of an unopposed extrusion of lymph from the surface of this hepatic lobe.

It is noteworthy that the total volume of fluid seen in these animals was much less than is seen regularly in animals with an abdominal liver and thoracic inferior vena cava constriction. There are several reasons for this discrepancy in total fluid production. The very marked adhesions which nearly regularly formed between the liver and the surrounding structures in the chest contain many vascular channels, both lymph and blood, and thus are able to carry these fluids away from the congested liver and into the lymphatic and capillary beds of the chest wall and other thoracic structures. This action is essentially an intrathoracic hepatopexy; also, large volumes of fluid cannot develop within the thoracic cavity of these animals because the volume of the cavity is markedly restricted by the presence of the large liver, and the rigid bony confines of the thoracic cavity prevent any accommodation to an expanding volume of fluid. Therefore, even moderate accumulations of fluid lead to pressure increases that cause pulmonary and cardiac embarrassment with relatively early death. In animals with abdominal livers and caval constriction, fluid continues to collect in the capacious peritoneal cavity, which is limited anteriorly and laterally by pliable muscular walls that yield to the pressure of the increasing fluid. Many liters of fluid are produced by these animals which may live for many months or even a year.

Some of our animals with complete thoracic livers accumulated moderate volumes of fluid within the peritoneal cavity. If liver lymph were the only source of this fluid, there would be none within the peritoneal cavity. We do not know the source of the small amounts of ascites in these animals. Perhaps lymphatic fluid is extruded from the very dilated lymphatic channels and the large, succulent nodes noted within the upper abdominal cavity in some of these animals. They appeared to be situated along the course from the liver to the cisterna chyli. Whether or not part of the ascitic fluid has its origin in weeping from the visceral and parietal peritoneum is not known.

Our experiment and the works of Mallet-Guy, Gage and his associates, and Freeman certainly implicate liver lymph as the primary source of experimental ascites. It is not known whether liver lymph has any relation to the pathogenesis of ascites in cirrhotic patients. Many surgeons have noted and commented upon the very large, dilated lymphatics within the porta hepatis and even droplets of fluid on the liver surface in patients operated upon for ascites secondary to cirrhosis. Theron and Allan presented microscopic sections of such livers showing markedly dilated subcapsular

lymphatics; they claimed that these dilated lymph spaces are not seen in cirrhotic livers without ascites. They and others have strongly recommended side-to-side or H type portacaval shunting procedures for the relief of this marked hepatic congestion and secondary ascites. Gliedman and Enquist and others have found the end-to-side portacaval shunt eminently satisfactory for the control of unrelenting ascites in these patients. It is probably true that the shunt does not affect the ascites production by any reduction in portal pressure but rather by relieving the congestion in a liver with a markedly constricted venous outflow and a slightly diminished dual inflow. After relief of congestion, weeping of lymph from the liver and possibly from the portal lymphatics no longer occurs.

SUMMARY

1. In 23 dogs the entire liver was moved into the chest, the diaphragm was repaired beneath it, and the inferior vena cava was constricted above the liver.

2. In most of the animals, more hydrothorax than ascites developed.

3. These findings and the results of other studies suggest very strongly that the source of experimental ascitic fluid is extruded hepatic lymph.

4. The possible relationship of these findings to the pathogenesis of hepatic ascites in clinical cases is briefly discussed.

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AN EVALUATION OF THE ONE STAGE, LOW ANTERIOR RESECTION

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MANY SURGEONS have written and taught that combined abdominoperineal resection in one or two stages is the only operation to be considered for a malignant lesion situated at the peritoneal reflection, involving the peritoneal reflection, or lying below the peritoneum. Thus, it is important to be informed concerning a surgical technique of low anterior resection by which the surgeon can get below the peritoneal reflection, resect a portion of the rectum, and preserve the anus and sphincters, with mortality, morbidity, and survival rates that compare favorably with those after sphincter-sacrificing procedures. Therefore, this study was undertaken to evaluate the one stage, low anterior resection without previous or concomitant colostomy, which is such a procedure. In making the evaluation, particular emphasis is given to length of hospitalization, mortality, postoperative complications, sphincteric function, and survival statistics.

MATERIALS AND METHODS

At the Mayo Clinic, from January 1935 through December 1958, the one stage, low anterior resection for cancer of the rectosigmoid or rectum or both has been performed on 362 patients who lived in this country. The case records and hospital charts of these patients were carefully studied, special note being taken of the preoperative proctoscopic reports on the level of the lesions and of the postoperative hospital course. Data concerning the gross and microscopic characteristics of these lesions were tabulated.

From personal communications at the time of follow-up examinations at the clinic or hospital and from letters received from physicians, patients, and relatives, it is possible to report on the status of 99.4 per cent of the 362 patients. Patients who, in the opinion of the surgeon, had palliative procedures because of palpable hepatic, metastatic lesions or malignant tissue that was not excised were considered separately when the long term results were studied. Survival statistics were calculated by the Section of Biometry and Medical Statistics of the Mayo Clinic.

From the Section of Surgery, Mayo Clinic, and the Mayo Foundation, Rochester.

AGE AND SEX

The youngest patient in the series was 25 years of age and the oldest was 92 years old at the time of operation. The average age for the entire group was 58.7 years; 45.5 per cent were 60 years of age or older. There were 195 men (53.9 per cent) and 167 women (46.1 per cent).

LOCATION OF THE LESION

Definite statements concerning the level of the lesions were recorded by the proctologist in 357 cases. At proctoscopic examination, a few lesions were measured from the dentate line rather than the anal margin. Three centimeters were added to those lesions which had been measured from the dentate line in order that all estimates would represent the distance from the anal margin to the lowest edge of the lesion. In no case was the lesion located more than 24 centimeters above the anal margin and in only 1 case was the lowest level of the lesion less than 5 centimeters from the anal margin. On proctoscopic examination, 76.7 per cent of the lesions in this series were located between 5 and 14 centimeters above the anal margin.

PATHOLOGIC ASPECTS

All of the lesions were adenocarcinomas except 1 which was a squamous cell carcinoma, grade 3 (Broders' classification) and type C (Dukes' classification), located 10 centimeters from the anal margin. The distribution of the lesions according to Dukes' classification was: type A, 24 patients (6.6 per cent); type B, 191 patients (52.8 per cent); and type C, 147 patients (40.6 per cent).

All lesions were graded on the basis of degree of microscopic cellular differentiation, according to Broders' method; 88.7 per cent were of grades 1 and 2 and 11.3 per cent were of grades 3 and 4. Venous involvement was noted in 46 cases (12.4 per cent) at the time of examination of fresh tissue, and in 34 of these 46 cases the lesions were of type C. Venous involvement associated with perineural lymphatic infiltration was found in 11 more of the 362 cases (3.1 per cent); in 10 of these 11 cases, the lesions were of type C. Infiltration of the perineural lymphatics was noted in an additional group of 11 cases (3.1 per cent); 8 of these lesions were of type C. Retrograde lymphatic spread was noted in 4 cases, at points 1.5, 3, 4, and 4 centimeters, respectively, distal to the lower edge of the lesion. Submucosal extension was noted 4 centimeters distal to the growth in 1 case and 8 centimeters proximal to the growth in another.

DISTANT METASTASIS

Operation was carried out as a palliative procedure in 58 of the 362 patients (16 per cent) because of either hepatic metastasis or extensive involvement of the surrounding viscera which made complete removal of the neoplastic process impossible.

OPERATIVE PROCEDURE

In earlier years covered by this study, intestinal antisepsis was created by the administration of sulfasuxidine. Within recent years, the preoperative sterilization of the bowel has followed the pattern described elsewhere (2).

The technical aspects of the operative procedure have been described previously (1) and will not be reviewed in detail. Two points should be emphasized, however: (1) the procedure used is the one stage, low anterior resection without previous or concomitant colostomy, and (2) anastomosis deep in the pelvis is technically impossible and unsafe without the aid of surgical instruments of proper length and shape. Instruments of this nature have been illustrated in a previous publication (1).

The cases reported are not considered as being specially selected, because low anterior resection is performed for any lesion whose lower border lies at 5 to 6 centimeters above the anal margin except when pronounced obesity renders it impossible to make the anastomosis. If the lower edge of the lesion is 5 to 6 centimeters from the anal margin, a low anterior resection with preservation of the anus is contemplated. However, before the operation, the patient is prepared for a one stage combined abdominoperineal procedure. The abdominal portion of the low anterior resection is performed in the same fashion as that of a one stage combined abdominoperineal resection, because the surgeon never knows what procedure is best until the growth has been mobilized. In starting the operation, he knows only that low anterior resection may be possible.

HOSPITAL DEATHS

Twenty-four deaths occurred in the hospital in this series of 362 patients, those after palliative procedures not excluded, giving a mortality rate of 6.6 per cent. Of those who died, 14 were men, 10 were women; their average age was 58.9 years, with extremes of 36 and 82 years of age. The causes of death were as follows: generalized peritonitis in 11 cases; pulmonary embolism in 5; acute coronary occlusion in 2; pseudomembranous ileocolitis in 2; uremia, with renal atrophy and cysts found at postmortem examination, in 1 case; peritonitis and jaundice, with ques-

TABLE I.—NONFATAL POSTOPERATIVE COMPLICATIONS IN 111 PATIENTS

Complication	*Patients*		
		No.	*Per cent of 338*
Fistulas		46	13.6
Colocutaneous	43		
Rectovaginal	3		
Urinary retention		28	8.3
Thrombophlebitis		21	6.2
Pelvic abscess		9	2.7
Prolonged ileus	6	8	2.4
Requiring operative decompression	2		
Separation of posterior anastomosis		4	1.2
Secondary closure of wound		4	1.2
Atelectasis or pneumonitis or both		4	1.2
Penicillin reaction		3	0.9
Psychiatric care needed		2	0.6
Nonfatal pulmonary embolus		2	0.6
Acute attack of arthritis		2	0.6
Gouty arthritis		1	0.3
Cerebrovascular accident		1	0.3
Acute attack of asthma		1	0.3
Myocardial infarction		1	0.3
Epididymitis		1	0.3
Parotitis		1	0.3
Hemorrhage from duodenal ulcer		1	0.3
Pulmonary edema		1	0.3
Rectal abscess		1	0.3
Balantitis		1	0.3

TABLE II.—FIVE YEAR SURVIVAL RATES ACCORDING TO PROCTOSCOPIC LEVEL OF LESION

Distance from anal verge, cm.	*Patients*		*Lived 5 yr. or more after operation*	
	Total	*Traced*	*No.*	*Per cent**
<5	1	1	1	—
5–9	57	56	28	50.0
10–14	95	94	61	64.9
15–19	29	29	18	62.1
20–24	9	9	7	77.8
Not stated	2	2	2	—
Total	193	191	117	61.3

*Based on traced patients. Inquiry as of 1 January 1959. Hospital deaths and palliative procedures are excluded in the calculation of survival rates.

tionable transfusion reaction, in 1; esophageal rupture, pneumonia, diabetes, and fibrillation in 1; and uncontrollable hemorrhage from esophageal ulcers, duodenal ulcer, and peritonitis in 1.

The proctoscopic levels of the lesions from the anal margin to the lowest level of the lesion in the 11 patients who died from peritonitis were as follows: 6 centimeters in 3 cases, 7 centimeters in 3, 8 centimeters in 2, 10 centimeters in 1, and 16 centimeters in 2.

HOSPITALIZATION AND POSTOPERATIVE COMPLICATIONS

The 338 patients who survived the operation were hospitalized for a minimum of 9 days to a maximum of 83 days, an average of 15.3 days. One or more nonfatal postoperative complications occurred in 111 cases (32.8 per cent) of the 338 living patients (Table I).

This may seem to be an excessive number of complications, but we have listed all and the great majority were of a relatively minor nature.

Fecal fistulas, the most common complication, occurred in 46 cases (13.6 per cent). Drainage subsided spontaneously before 35 of these patients (76.1 per cent) were dismissed from the hospital. Hospitalization of these patients extended from 16 to 80 days with an average of 28.1 days. Many of the 35 patients had associated complications which necessitated prolonging their hospitalization. The average hospitalization, however, was only 23.6 days for those patients with fecal fistulas alone (10 of the 35). In an additional 5 cases (10.9 per cent), the drainage ceased spontaneously in 52 days to 2 years from the time of operation; thus, spontaneous closure occurred in 40 of the 46 cases (87 per cent). A temporary diverting colostomy was made in 3 cases (6.5 per cent) and 2 of these patients later refused closure of the colonic stomas. The fistulas persisted until death in the remaining 3 of the 46 cases (6.5 per cent).

Urinary retention, the next most common complication, occurred in 28 patients (8.3 per cent). Sixteen responded to conservative treatment, and 12 required transurethral prostatic resection. Most of these 12 patients had a preoperative history of voiding difficulties.

Thrombophlebitis of the lower extremities was a rather frequent complication; it was encountered in 21 patients (6.2 per cent). Two additional patients experienced nonfatal pulmonary emboli and both lacked preceding episodes of thrombophlebitis. Thromboembolic phenomena, therefore, occurred in 7.7 per cent of the 362 patients when the 5 immediately postoperative deaths which resulted from pulmonary emboli are included.

TABLE III.—FIVE YEAR SURVIVAL RATES ACCORDING TO LEVEL OF LESION AND METASTASIS

Distance from anal verge, cm.	No metastasis				Metastasis			
	Patients		Lived 5 yr. or more after operation		Patients		Lived 5 yr. or more after operation	
	Total	Traced	No.	Per cent*	Total	Traced	No.	Per cent*
<5	1	1	1	—	—	—	—	—
5–9	35	34	22	64.7	22	22	6	27.3
10–14	64	64	50	78.1	31	30	11	36.7
15–19	16	16	11	68.8	13	13	7	53.8
20–24	8	8	7	87.5	1	1	0	—
Not stated	2	2	2	—	—	—	—	—
Total	126	125	93	74.4	67	66	24	36.4

*Based on traced patients. Inquiry as of 1 January 1959. Hospital deaths and palliative procedures are excluded in the calculation of survival rates.

SPHINCTERIC FUNCTION

On dismissal from the hospital, the patients were instructed to report on their progress after having been at home for 3 weeks and again after having been at home for 6 weeks. Re-examination was recommended 6 months after operation. Evaluation of sphincteric function was estimated at the time of examination 6 months after operation except in the few cases in which 6 months had not elapsed since operation or in which there were recurrences before the 6 month period had elapsed. In these cases, sphincteric action was evaluated from the reports made 3 and 6 weeks after operation. The 24 postoperative deaths were excluded. Sphincteric function was classed as good when the patient considered his bowel control and bowel habits the same as before operation. In 278 patients (82.2 per cent) the results were good. Forty-six of the 278 patients (13.6 per cent of the 338) had a pronounced tendency to constipation.

The results were designated as fair when the only complaint was rectal frequency with 5 to numerous evacuations each day. Thirty-seven patients (10.9 per cent) had fair sphincteric function 6 months after operation. Seven of them (18.9 per cent), however, could be placed in the group with good results 1 to 4 years after operation. One of the 37 patients (2.7 per cent) had episodes of frequency and diarrhea only after eating certain foods. In 8 (21.6 per cent) of the 37, bowel habits were altered as a result of treatment of local recurrences with radium, roentgen rays, or fulguration, alone or in combinations, and the alteration was not considered to be due directly to the initial operation.

The results were considered to be poor if rectal incontinence or soiling required the wearing of a perineal pad. In 19 patients (5.6 per cent) the sphincteric result was poor. With the use of perineal exercises and regulation of the diet and after passage of time, the incontinence of 7 of these 19 patients (36.8 per cent) abated in 3 months to 4 years. In 6 of the 19 (31.6 per cent) the incontinence followed treatment with radium or roentgen rays or by fulguration for local recurrences or all three, and in 2 (10.5 per cent) it was noticed only after dietary indiscretions.

Of the remaining 4 patients in the series, 1 (0.3 per cent) died within 4 months; 2 required diverting colostomy because of fecal fistula and 1 because of rectal stricture.

SURVIVAL

Of the 362 patients in this study, 250 underwent operations 5 or more years ago. Of the 250 patients, 18 died during hospitalization and 39 underwent operation designated as palliative. Only 2 patients were untraced during the subsequent 5 year period. The 5 year survival rate of the 230 traced patients, excluding 18 who died in the hospital, was 52.2 per cent. Hereafter, the 39 patients who had palliative operations are excluded from analysis of survival. Of the remaining 191 traced patients, 117 (61.3 per cent) have survived 5 or more years (Table II). Ninety (59.6 per cent) of 151 traced patients with lesions in the controversial segment—the lower level of the

lesions not exceeding 14 centimeters from the anal margin—survived 5 or more years after operation.

The results were analyzed in an effort to correlate prognosis with the presence or absence of malignant invasion of lymph nodes at various proctoscopic levels (Table III). Of the patients without nodal metastasis, 74.4 per cent lived 5 or more years, and of those with metastasis, 36.4 per cent lived 5 or more years. Of patients with lesions in the controversial zone, 73 (73.7 per cent) of 99 traced patients without involved nodes survived for a minimum of 5 years, and 17 (32.7 per cent) of 52 traced patients with involved nodes survived for a minimum of 5 years.

Of the 46 patients who had venous involvement 32 are dead, 30 within 5 years of the operation; 1 lived for 9 years; and 1 for 5 years after operation. Nine of the 11 traced patients in whom perineural lymphatic and venous invasion was noted at the time of operation died before 5 years had elapsed. Of the 11 traced patients who had perineural lymphatic invasion, 10 died before 5 years had elapsed; the other patient is living 10 years after operation.

Of the 362 patients in this study, only 73 underwent operations 10 or more years ago. One patient was untraced during the subsequent 10 year period. Four patients died during hospitalization and 11 underwent operation designated as palliative. The 10 year survival rate of the 68 traced patients, excluding 4 hospital deaths, was 43.5 per cent. If the 11 palliative cases are also excluded from the survival analysis, then of the remaining 57 patients, 30 (52.6 per cent) have survived 10 years.

SUMMARY

Follow-up data have been presented on 362 patients with carcinoma of the rectum or rectosigmoid or both who have undergone one stage, low anterior resection.

Twenty-four patients died in the immediate postoperative period, giving a hospital mortality rate of 6.6 per cent.

Hospitalization of the remaining 338 patients averaged 15.3 days.

The postoperative complications which occurred most frequently were fecal fistulas (13.6 per cent), urinary retention (8.3 per cent), and thrombophlebitis (6.2 per cent).

Satisfactory sphincteric function resulted in 93.2 per cent of the cases.

When the hospital deaths and palliative procedures were excluded, the 5 year survival rate was 61.3 per cent and the 10 year survival rate was 52.6 per cent.

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POSTOPERATIVE CONVALESCENT TIME

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To REDUCE the number of days lost to illness by members of our society seems to have medical, social, and economic merit. One method of attaining this goal is to return a patient to normal full activity as early as practicable after operation or an illness. To overextend a convalescence is just as wasteful and just as imprecise and unscientific medical practice as to shorten convalescence to a point where the patient is unable to perform his required tasks.

Recent studies revealed rather wide discrepancies between groups studied as to the period of convalescence between certain common surgical procedures and normal full activity. The evidence previously reported (4) suggests that the Air Force returns men to duty after a convalescence only half as long as that required by comparable civilian patients. Although various possible explanations for these findings were suggested in that report, it was thought that additional evidence should be obtained. In order to consider the subject of the optimum time to return to full normal activity, studies must be made of several series of patients to determine the advantages and disadvantages of the regimen followed in each series.

In the present investigation the facets studied were the effect on the patient of this earlier return to work, whether this "early return" was real or only apparent because of sheltering of the returnee by his supervisor, and if examination of other data would substantiate the earlier findings.

To get information for study, a letter of introduction and a questionnaire were sent to patients discharged from the General Surgical Service at the United States Air Force Hospital at Lackland who had had one of the following five operative procedures: inguinal hernioplasty, appendectomy, hemorrhoidectomy, tonsillectomy, or pilonidal cystectomy. The survey covers operations performed during 1957, 1958, and 1959. As in the previous study, only the uncomplicated cases were used in determining the average length of hospitalization. Five hundred and eighty-three patients' records have been reviewed, and a letter of inquiry has been sent to each patient. Two hundred and eighty-five of these questionnaires were returned with complete enough information to permit inclusion in this study.

Comparison of the present findings of the number of days lost after operation with two previous Air Force series is made in Table I. The difference between these series is about 10 per cent, but significantly less than the difference between Air Force average number of days lost and the loss noted in civilian studies. It is possible that the difference between these studies represents the difference between a large hospital experience with a preponderance of off-base patients and a total Air Force experience which is, in the main, based on small hospital experience with most of the patients coming from on-base. Patients who are referred from smaller bases to a large general hospital are more likely to be those in whom some complicating factor exists, circumstances such as marked overweight, large size of the hernia, or a long history of repeated trouble with hemorrhoids. These factors, while not picked up in a statistical survey as complications, are prone to prolong the hospitalization period because of the more extensive surgical procedure required or the apprehension they induce in the re-

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TABLE I.—COMPARISON OF DAYS LOST AFTER OPERATION IN PRESENT AND PREVIOUS SERIES

Operation	*No. of days hospitalized postoperatively, Lackland series*	*No. of days hospitalized postoperatively. Earlier Air Force-wide series*	
		*1956**	*1958†*
Tonsillectomy.....	5.6	7.7	5.2
Inguinal hernioplasty	19.9	18.9	13.0
Appendectomy.....	15.8	13.5	12.3
Hemorrhoidectomy..	19.2	13.0	10.1
Pilonidal cystectomy.	30.5	31.5	

*Series reported by Wenger.
†Series reported by Gold.

sponsible surgeon. It is also true that a physician is more likely to retain a patient an extra day or so if he knows the patient is to return to a base some hundreds of miles away instead of to the local base where the responsible surgeon will be available in case the patient has a problem or questions.

The earlier Air Force report (4) gave the period of postoperative hospitalization as the period of convalescence. It was quite properly questioned whether this was a true representation of the facts. To determine if patients actually returned to full duty when dismissed from the hospital, patients in this series were followed up and interrogated as to their activities. The results tabulated in Table II show that the "early return" reported was accurate in 90 per cent of the patients reported on. It is worthy of emphasis that those patients who went to "full duty," did exactly that. This means that the basic airman went back to his strenuous physical program, the supply sergeant went back to work in his supply room, and the pilot went back to flying. In this case "duty" does not mean merely dropped from the hospital rolls and returned to the parent organization, it means going back to work at his usual job. In the 10 per cent who were reported as returned to duty but who did not actually go to full duty, it must be stressed that they did go to work, but their usual daily work was modified with some of the more strenuous elements removed. For example, the basic airman avoided the obstacle course for a few days. This situation usually results when a supervisor makes his own decision that the new returnee is not ready for work, in spite of the contrary decision of the physician who returned the man to duty. It is of course possible that the returnee has influenced the supervisor to assume this benevolent attitude. It has been pointed out to us by Dohan that this same problem exists in industry and that a percentage of those workers returned to work are carried on light duty for a while because of the opinion of the supervisor that a little more "rest" will do the patient good.

TABLE II.—NUMBER RETURNED TO FULL DUTY AT END OF HOSPITAL CONVALESCENCE

Operations	*No. of patients*	*No. to full duty*	*Per cent to full duty*
Tonsillectomies.....	34 (all adults)	30	89
Inguinal hernioplasties.	116	104	89
Appendectomies.....	79	71	89
Hemorrhoidectomies...	31	28	90
Pilonidal cystectomies..	25	24	90
Totals.....	285	257	90

Of the 28 patients who did not return to full duty upon discharge from the hospital, study was made of each record and a determination made of the additional number of days lost. If these days are treated as completely lost, although they were not because some duty was being done, a total of 233 more days must be added to the total number of lost days. This amounts to almost exactly 4.5 per cent which may be used as a correction factor on the original figures. Adding this 4.5 per cent correction factor to our reported figures in this series, results are as tabulated in Table III.

Previous studies have determined the number of days lost according to age groups in the effort to determine if age was a significant factor. Saffeir showed that age was of little significance, the average period of time lost after surgical procedures being only a week longer in a 65 year old male than in a 25 year old male. In our study, the number of days lost when broken down into decades showed no significant differences between the age groups. Our results are given in Table IV. These results are

the same as those obtained in a previous study in 1956 (4) made upon a world-wide statistical sample of Air Force experience. The fact that the present series is an all male series needs to be recorded.

The final facet to be studied is that of the effect on the patient of this earlier return to work. Of the 34 patients with tonsillectomies studied, 3 (10 per cent) said that they were tired or weak for a few days. The only other complaints were of a minor sore throat or hoarseness. Seventy-one per cent had no symptoms at all after discharge. This series includes all servicemen, no children. Of the 4 patients who did not return to full duty upon discharge from the hospital, the work of 3 required shouting (control tower operator and training instructors), and the fourth had a minor reaction to penicillin after leaving the hospital. His case was not tabulated as a complication and hence omitted from this series because his reaction did not occur until after he had been returned to duty.

Seventy-three per cent of the patients who had hernioplasties thought that their hospital discharge was properly timed. Twenty per cent, or 1 out of 5 patients, reported difficulty in heavy lifting immediately after leaving the hospital. Intermittent pain in the operative site was described by the same number, in 1 case for as long as 8 months. In this series of 116 hernioplasties 1 recurrence was found, a rate of 0.86 per cent. This occurred in an 18 year old airman who had been hospitalized for 16 days and returned to duty. His duty consisted of being an administrative clerk, and on occasion he was in charge of the Transient Airman's Quarters. He made a special effort to point out that he did do "KP" when requested. Since he left us he has had 4 more operations for hernia and an appendectomy. Of those 12 patients who did not go to full duty upon discharge from the hospital, 2 were officers who were grounded by their flight surgeons for reasons obscure to us. One patient was separated from the service upon discharge from the hospital for reasons unrelated to the hernia repair. The rest of the group, 9 patients, were basic airmen who had an extremely arduous program and were therefore excused from the most violent portion of their activities for a short time.

TABLE III.—COMPARISON OF POSTOPERATIVE DAYS LOST IN VARIOUS GROUPS

Operations	*Lackland series (4½ per cent correction added)*	*U.S.P.H.*	*Traveler's Insurance Co. 1958*	*Large industry*
Tonsillectomies.....	5.8	9.1		13.2
Inguinal hernioplasties	20.8	72.9	46	51
Appendectomies.....	16.6	19.3	35	32 (male)
Hemorrhoidectomies..	20.6	33.6	28	36
Pilonidal cystectomies.	31.9	—	—	—

All patients in this study have been followed up for periods of from 6 months to 3 years; however, the follow-up period seems of most importance in connection with the patients who had hernioplasties.

Of the 79 patients who underwent an appendectomy, two-thirds had no symptoms after discharge from the hospital and the rest, when directly interrogated, said that they had some wound tenderness and passing difficulty with physical training programs. One patient complained of easy fatigability.

Sixty-one per cent of the 31 patients who underwent hemorrhoidectomy had no symptoms after discharge from the hospital. The others had a little bleeding or tenderness, but it was not disabling.

Sixty per cent of the 25 who underwent pilonidal cystectomy had no ill effects. The other 40 per cent had a variety of minor complaints, such as difficulty in sitting,

TABLE IV.—AVERAGE NUMBER OF DAYS LOST COMPARED BY DIAGNOSIS AND AGE GROUP

Operations	*Age in years* 10–19	20–29	30–39	40–49	50–59
Tonsillectomy.....	6.3 (6)	5.7 (22)	6.0 (5)	2.0 (1)	
Inguinal hernioplasty.	17.6 (38)	21.6 (56)	19.8 (12)	23.0 (9)	21.0 (2)
Appendectomy.....	14.2 (34)	15.4 (40)	19.6 (5)	14.0 (2)	
Hemorrhoidectomy...	15.0 (2)	18.5 (18)	21.5 (8)	10.7 (4)	

( )=No. of cases in sample.

marching, and lifting. Eight per cent of this group had recurrence which is believed to be unrelated to the time of return to duty.

DISCUSSION

The data gathered in this study support the facts given in the earlier reports as to the average length of postoperative period before return of patients to normal full activity and also support the use of the figure for the postoperative hospital stay in the Air Force as equivalent to the interval from operation to full duty. In 90 per cent of the cases it was completely accurate. The error introduced by the patients who did not return to full duty amounts to 4.5 per cent. Using this factor to correct our figures makes little difference in the final amount of time lost by Air Force patients after operation. Thus, the conclusions drawn in the earlier reports are valid. The 8 per cent recurrence rate of pilonidal cysts, the 0.86 per cent recurrence rate of hernias, and the absence of other complications support the conclusions that there was no untoward effect on the patient as a result of early return to work.

Moss and Dohan have reported that most of their patients complained of increased fatigue for the first week after returning to full activity. Our survey does not reveal such a high incidence of fatigue. Those with the highest incidence of fatigue were the patients who had tonsillectomies. Of these, 9 per cent had such a complaint. Speculation as to the reason for the difference in reported fatigue suggests a possible difference in method of interrogation. Dohan asked specifically about fatigue whereas we asked only about ill effects and whether the patient thought that the return to duty was timely. The patients in the present series returned to duty earlier than those in the series reported by Moss and Dohan, and one wonders whether this earlier return to normal activity is a significant factor in the lower incidence of fatigue in the Air Force group.

SUMMARY

In Air Force practice the number of postoperative days of hospitalization is a practical equivalent of the actual number of postoperative days of convalescence. A study of a series of 285 patients undergoing one of five common surgical procedures substantiates the fact that Air Force patients return to full activity after one-half the convalescent period experienced by comparable groups of civilian patients. This early return to full activity results in no harm to the patient.

The saving of one-half of convalescent time after operation is a significant matter. It represents a saving in man-hours and money and may actually increase the patient's well-being rather than be a hazard to him.

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PORTAL HYPERTENSION AND BILIARY CIRRHOSIS

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CIRRHOSIS OF THE LIVER with portal hypertension has been the subject of many recent articles. Most investigators agree that a patent portal systemic shunt effectively controls bleeding from esophageal varices. Obviously, when this immediate threat to life is reduced, concern should be focused on the natural history of the underlying hepatic disease. Emphasis is offered of the need for proper classification of the coexisting hepatic disturbance in the evaluation of long term survival after portal systemic shunting procedures.

The group of diseases which comprise the entity of biliary cirrhosis is particularly suited to illustrate this concept because in some types the cause is surgically correctable. Thus, not only can the portal hypertension be reduced, but the course of the hepatic disease can be altered. In others, however, the hepatic disease is progressive, regardless of reduction in portal pressure. In the surgical literature, infrequent mention is made of biliary cirrhosis as a cause of portal hypertension. However, occasional reports by others indicate that as many as 50 per cent of patients with biliary cirrhosis have associated esophageal bleeding and portal hypertension. Thus, it is apparent that this disease can and does result in death from hemorrhage.

The nomenclature of the various types of biliary cirrhosis is confusing, as the following partial list indicates:

Primary biliary cirrhosis
Secondary biliary cirrhosis
Hanot's cirrhosis
Xanthomatous biliary cirrhosis
Pericholangiolitic biliary cirrhosis
Cholangiolitic biliary cirrhosis
Cholangitis lenta
Intrahepatic cholangiolitic biliary cirrhosis
Interstitial chronic hepatitis with liver hypertrophy
Nonobstructive cholangitic biliary cirrhosis
Chronic intrahepatic obliterating cholangitis

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The terms primary and secondary often are used to differentiate intrahepatic and extrahepatic causes, but may also be used to distinguish the idiopathic group (primary) from those cases of biliary cirrhosis in which the cause is known (secondary). The remaining terms either refer to the microscopic picture or to a distant manifestation of the disease, such as xanthomatosis, or are eponymic. The following classification is suggested as being more descriptive of the etiology of the disease.

Group I. Biliary cirrhosis due to intrahepatic obstruction
1. Cholangiolitic cirrhosis
   a. Viral
   b. Drugs
   c. Idiopathic
2. Xanthomatous biliary cirrhosis
3. Biliary cirrhosis secondary to mucoviscidosis
4. Biliary cirrhosis secondary to atresia of intrahepatic bile ducts (acholangic biliary cirrhosis)

Group II. Biliary cirrhosis due to extrahepatic obstruction
1. Congenital (atresia of extrahepatic bile ducts and choledochus cyst)
2. Inflammation (intraductal or extraductal leading to stricture)
3. Neoplasm (intraductal or extraductal)
4. Trauma (especially surgical)

The following cases were selected to illustrate certain types of biliary cirrhosis and emphasize their various clinical courses.

CASE 1. This was a case of slowly progressive cholangiolitic cirrhosis with hemorrhage. In 1953, a 68 year old housewife, who had been previously well, experienced her first episode of hematemesis. She was hospitalized elsewhere for this complaint on 4 sepa-

rate occasions, only once requiring blood transfusion. In 1955, she underwent a hemorrhoidectomy. At that time, an esophagram revealed a large esophageal diverticulum but no varices. Esophagoscopy was attempted but abandoned after failure to circumvent the diverticulum. The patient was admitted to Jefferson Medical College Hospital in September 1956 for removal of this lesion. At this time, the chief complaint was difficulty in swallowing food, regurgitation of previously ingested food on reclining, and a 40 pound weight loss.

On examination, the only positive finding, other than obvious cachexia, was hepatomegaly. It was believed that the patient was too malnourished to tolerate removal of the diverticulum. A Stamm gastrostomy was performed on 28 September 1956 for feeding purposes. Two weeks later, the patient had a massive hematemesis and quickly died despite transfusions and tamponade of the lower esophagus by an esophageal balloon.

Postmortem examination revealed multiple large esophageal varices with evidence of recent hemorrhage, idiopathic cholangiolitic cirrhosis, and congestive splenomegaly.

CASE 2. This was an instance of rapidly progressive cholangiolitic cirrhosis with hemorrhage. An episode of painless jaundice for 1 month in May 1957 was the first sign of hepatic disease in a 48 year old woman. Since that time, she noted loss of appetite, generalized weakness, and loss of weight. Three days before admission, she vomited bright red blood. This recurred on 6 occasions in the ensuing 24 hours and she was admitted to another hospital. She required 7 pints of blood in order to stabilize her pulse and blood pressure and was transferred on 17 October 1957 to the Jefferson Medical College Hospital for definitive treatment of the bleeding.

On admission, she was comatose. Her blood pressure was 130/70 and her pulse 120. She was obviously jaundiced and her liver and spleen were moderately enlarged.

Shortly after her arrival, she vomited approximately 2,500 cubic centimeters of bright red blood. Esophageal tamponade was begun and the bleeding controlled. She was given intravenous fluids, neomycin through the Sengstaken-Blakemore tube, cleansing enemas, and 5 pints of blood. Although there was no further evidence of gastrointestinal bleeding, her condition rapidly deteriorated and she died 3 days after admission. Postmortem examination revealed idiopathic cholangiolitic cirrhosis. There were extensive esophageal varices. Cause of death was ascribed to hepatic failure.

CASE 3. This was a case of cholangiolitic cirrhosis and portal hypertension, without hemorrhage. In August 1955, a 66 year old white woman was admitted to the Jefferson Medical College Hospital with a history of progressive jaundice of 6 months' duration. In addition, she stated that she had an attack of painless jaundice 31 years previously. Five weeks prior to admission, she noted swelling of her abdomen and ankles. There was no history of alcoholic intake. On physical examination, the patient was icteric and there was obvious ascites. The liver and spleen were markedly enlarged. Hepatic function studies were consistent with a diagnosis of extrahepatic biliary obstruction. An exploratory laparotomy revealed an enlarged, greenish, nodular liver with a normal extrahepatic biliary tree. The spleen was enlarged. A biopsy of the liver was performed and sections revealed cholangiolitic biliary cirrhosis. Postoperatively, her jaundice increased and there were signs of progressive liver failure. She died 1 week after operation. Postmortem examination confirmed the operative findings. In addition, the esophagus contained extensive varices which apparently had not bled.

The commonest cause of death from biliary cirrhosis is hepatocellular failure followed in frequency by exsanguination from esophageal varices. Biliary cirrhosis without extrahepatic obstruction is characterized by an insidious onset. Pruritis is usually the initial symptom and is accompanied by the gradual development of jaundice. The liver is always enlarged, as is the spleen in 80 per cent of cases. Chemically, the picture is one of biliary obstruction. In a recent interview, Sherlock summarized the course of 42 patients with biliary cirrhosis of intrahepatic origin. Twenty-three of these patients died within 5 years of the onset of the disease, 15 from hepatocellular failure and 6 from bleeding esophageal varices.

If the correct diagnosis had been made in the first case at the time of the initial hematemesis and a portal-systemic venous shunt established, the patient probably would not have died of recurrent hemorrhage. Case 2 is representative of rapidly progressive intrahepatic biliary cirrhosis. The episode of bleeding undoubtedly precipitated further hepatic deterioration which led to the patient's death. It is unfortunate that the bleeding was not controlled immediately after its onset. If she had survived the immediate posthemorrhage period, hepatic function could have been evaluated and a shunt considered. In Case 3, the patient had esophageal varices, there were no

episodes of bleeding, and she died of uncomplicated hepatic disease. Of these 3 patients, the first undoubtedly would have benefited from a portacaval shunt, the second might have benefited but probably would not have, and, in the third, evidence of portal hypertension was never noted during life.

CASE 4. This was a case of cholangiolitic cirrhosis with hemorrhage, treated by portacaval shunt. The first symptom of illness in a 45 year old woman occurred when severe pruritis developed. Four years later, she experienced her first episode of hematemesis and melena. She was admitted to another hospital and given supportive treatment. During the following 8 months, there were 3 separate episodes of hematemesis, 2 requiring blood transfusions for stabilization.

In September 1958, she was admitted to Jefferson Medical College Hospital at which time there was no evidence of bleeding. There was no history of hepatitis and no history of excessive intake of alcohol. There was a definite bronze pigmentation of the skin. The liver and spleen were both enlarged. Laboratory studies included a serum bilirubin level of 29.6 milligrams per cent, and the alkaline phosphatase was 38.9 Bodansky units. A cholecystogram revealed a normally functioning gallbladder with no evidence of gallstones. A splenoportogram demonstrated gastric and esophageal varices. On 13 November 1958, an end-to-side portacaval anastomosis was performed. The pressure measured in an omental vein was 60 centimeters of water before completion of the shunt and 12 centimeters thereafter. A biopsy of the liver performed during the procedure showed biliary cirrhosis of the cholangiolitic type. Her postoperative course was uneventful.

She has now been followed up for 1 year with no evidence of bleeding. The bronzed color of her skin persists but she has gained weight and feels well.

CASE 5. This was a case of cholangiolitic cirrhosis with hemorrhage, treated by portacaval shunt. A 68 year old nun first experienced hematemesis in 1949. There was no history of hepatitis or alcoholic intake. Intermittent recurrences developed until 1955. At this time she was admitted to another hospital where she underwent esophagoscopy. Varices were noted and injected with sclerosing agents. Because of recurrent bleeding, she underwent transesophageal ligation of the varices in December 1956. In February 1957, further bleeding occurred and a splenorenal venous anastomosis was performed. In spite of this, she bled again on at least 6 occasions. She was hospitalized on October 1958 and required 5 pints of blood to stabilize her blood pressure. Esophageal varices were again demonstrated roentgenographically. Liver function studies were excellent. A portacaval shunt was advised but refused. On 1 December 1958, another massive hemorrhage occurred and she was admitted to Jefferson Medical College Hospital.

On physical examination, her mucous membranes, conjunctivae, and palms were very pale, with no evidence of jaundice. The liver edge was barely palpable. The admission hemoglobin was 5.8 grams, and the hematocrit was 19 per cent.

On 9 December 1958, a portacaval anastomosis was performed. Pressure in the caval system was reduced from 45 to 22 centimeters of water after completion of the shunt. Postoperatively, her cardiac rate increased to 152 per minute with a diastolic gallop rhythm. She was thought to be in left ventricular failure and was rapidly digitalized. Two days later, she suddenly died. Postmortem examination revealed extensive esophageal varices. The portacaval anastomosis was patent. Histologic examination of the liver revealed biliary cirrhosis with no evidence of extrahepatic biliary disease. The cause of death was cardiac failure.

These patients also had biliary cirrhosis of intrahepatic origin. The fact that they survived multiple episodes of esophageal hemorrhage indicated excellent hepatic reserve. The establishment of a portacaval anastomosis in Case 4 was accomplished without difficulty. The patient's postoperative course was uncomplicated. According to Sherlock, 70 per cent of patients with cholangiolitic biliary cirrhosis will survive longer than 5 years if no bleeding occurs. By control of esophageal hemorrhage, this patient falls into this more favorable category.

Cases 4 and 5 are similar in the progression of the hepatic disease. In Case 5, however, multiple inadequate operations were performed in an attempt to prevent further hemorrhage. If a properly constructed portacaval shunt had been carried out following the initial hematemesis 9 years before, it is quite possible that the patient's course would have been similar to that of the patient in Case 4 in spite of their age differences.

CASE 6. This was a case of biliary cirrhosis secondary to mucoviscidosis. A 13 year old girl with steatorrhea of 2 months' duration was admitted to the Jefferson Medical College Hospital on the service of Dr. C. W. Wirts. She had had pneumonia twice as a child and had a chronic cough. She had been hos-

pitalized on 3 occasions for "dehydration" during the summer months.

She was underweight, pale, and appeared malnourished. Her abdomen was protuberant. On examination, and by roentgenography, a bilateral pneumonitis was evident. A roentgenogram of the small bowel demonstrated puddling and coarseness of the mucosa. A glucose tolerance curve was diabetic in type. Duodenal drainage revealed no tryptic activity. Excess neutral fats and undigested meat fibers were found in the stools. She was treated with antibiotics, her pneumonitis resolved, and she was discharged with pancreatic replacement therapy.

During her sixteenth to nineteenth years, she was readmitted to the hospital on 6 more occasions with essentially the same problem. Her last admission to the hospital was at the age of 20 years. She complained of severe dyspnea and vague chest pains. She had a temperature of 103 degrees and was cyanotic. Her abdomen was still distended. For the first time, she had hepatomegaly. A bilateral pneumonitis was again present. An electrocardiogram revealed cor pulmonale. Her sputum was thick and tenacious. In order to facilitate tracheal aspiration, a tracheal fenestration was performed. Despite vigorous medical treatment, she finally died.

Postmortem examination revealed extensive fatty degeneration of the pancreas with fibrosis and cysts. The lungs showed severe bronchiectasis with bilateral bronchopneumonia and abscesses. Biliary cirrhosis due to intrahepatic obstruction was noted, and there were esophageal varices.

Biliary cirrhosis associated with cystic fibrosis of the pancreas has been described by di Sant'Agnese and Blanc. They stated that a "child with the syndrome of portal hypertension secondary to cirrhosis of the liver has one chance in two of having cystic fibrosis of the pancreas." Five cases were described with this syndrome associated with hemorrhage from esophageal varices. The case presented represents an unusually long survival with mucoviscidosis. Shunting to control hemorrhage in this type of case certainly will have no effect on the underlying disease.

CASE 7. This was a case of biliary cirrhosis secondary to surgical trauma. A 55 year old woman was well until June 1956, when acute cholecystitis developed, and she was admitted to another hospital where a cholecystectomy was performed. On the third postoperative day, she became jaundiced. She was discharged from the hospital 1 week postoperatively and underwent periodic examination by the operating surgeon for 1 year. During this interval, the jaundice became more pronounced and her urine became very dark. Severe anorexia developed, and she lost 43 pounds. One year from the time of cholecystectomy, she underwent an exploratory laparotomy by another surgeon at this same hospital, but the common duct could not be located. She was referred to a second hospital and was again operated upon. A divided common duct was found and repaired by end-to-end anastomosis. At this time, the patient had advanced biliary cirrhosis. A T-tube cholangiogram revealed patent extrahepatic biliary ducts, but her jaundice persisted. In December 1957, she became progressively lethargic and was admitted to Jefferson Medical College Hospital on 17 January 1958. On physical examination, the pertinent findings were those of pronounced jaundice and cachexia. The patient was semicomatose. The abdomen was distended, and the liver and spleen were enlarged. She exhibited hyperactive deep tendon reflexes and typical "flapping" of the upper extremities. Laboratory data were consistent with severe hepatocellular damage. A T-tube cholangiogram again demonstrated a patent extrahepatic biliary ductal system.

On 4 February 1958, she had massive hematemesis and lapsed into coma. Despite control of bleeding with a Sengstaken-Blakemore tube, transfusion of 3,000 cubic centimeters of blood and vigorous treatment of hepatic failure, she died on 8 February 1958.

Postmortem examination revealed advanced biliary cirrhosis secondary to the previous obstruction of the extrahepatic biliary system. In addition, there was acute esophagitis, ulcerated esophageal varices, and evidence of massive hemorrhage. The spleen was enlarged and congested.

An unfortunate combination of operative error compounded by negligence in the case of this woman allowed severe biliary cirrhosis to develop. The case illustrates that some types of biliary cirrhosis with esophageal hemorrhage have an underlying correctable cause. Early in the disease, correction of the extrahepatic biliary obstruction would have prevented the development of biliary cirrhosis and portal hypertension. Late repair of the common duct injury may arrest the cirrhotic process before the onset of portal hypertension. Eventually, severe hepatocellular damage occurs with obstruction of the bile ducts, and the process becomes irreversible.

DISCUSSION

The majority of patients treated by the establishment of a patent portal systemic

shunt do not have a recurrence of esophageal bleeding. The determining factor in the patient's long term survival then becomes the underlying hepatic disease.

In portal cirrhosis, the course after shunting is slow progression of the hepatic disease and eventual hepatic insufficiency. Blakemore has stated that a reduction in portal venous pressure has a beneficial effect on the course of the portal cirrhotic process. However, this fact has not been established. The exact mechanism for the development of portal hypertension in portal cirrhosis is not known. Most investigators agree, however, that portal hypertension is a manifestation of obstruction to the flow of portal venous blood by periportal fibrosis and pressure from regenerating hepatic nodules.

Biliary cirrhosis is not a single disease entity, but, rather, a late manifestation of many diseases. The common factor is obstruction to the flow of bile in either the extrahepatic ductal system or the finer intrahepatic biliary radicles. Bile stasis produces a periportal inflammatory reaction with eventual fibrosis. The resultant obstruction to portal venous blood flow is then similar to that produced in Laennec's or postnecrotic cirrhosis. McMahon and Thannhauser state that portal hypertension develops late in the course of biliary cirrhosis. Doehlert and co-workers explain this on the basis of slow hepatic regeneration. The disease process can progress quite rapidly as evidenced by Cases 2 and 3. These patients died within 6 months of the onset of symptoms with extensive esophageal varices.

We have suggested a classification of the various types of biliary cirrhosis which is descriptive of the etiology. Group I includes the causes of intrahepatic biliary obstruction. Portal hypertension has been reported in each of these types. Five cases of cholangiolitic cirrhosis have been presented. In each of these patients portal hypertension and esophageal varices developed. In Cases 4 and 5 the patients were treated with a portacaval shunt. There was one satisfactory result with survival without recurrence of esophageal bleeding and no further deterioration of hepatic function at the time of this report. The other patient died in the postoperative period of cardiac failure. Ricketts and Wissler reported a similar case with survival but no follow-up data. Kunkel, in an extensive review of biliary cirrhosis, reported 3 out of 4 successful results after portacaval shunting for cholangiolitic cirrhosis with esophageal hemorrhage. One patient died of cholemia 4½ years after the operation. The remaining 2 survivors showed evidence of slow progression of the hepatic disease but no further hemorrhage. Kunkel concluded that portal systemic shunts are of definite value in prolonging life but do not affect the underlying hepatic disease. Myers and his group reported a case in which xanthomatous biliary cirrhosis and portal hypertension developed after chlorpromazine therapy. Case 6 is an example of biliary cirrhosis and portal hypertension secondary to mucoviscidosis. Gross, in 1953, described the use of splenorenal shunts in 4 children who had biliary cirrhosis secondary to intrahepatic biliary atresia. All were still living from 5 months to 3 years at the time of his report.

Biliary cirrhosis due to extrahepatic obstruction (group II), on the other hand, may be amenable to surgical relief of the obstruction. If esophageal bleeding has occurred and is controlled by a shunt, surgical treatment of the biliary obstruction could affect the course of the underlying hepatic disease, depending upon the stage of the disease. If many cases are accumulated within this etiologic classification, meaningful data may be obtained about the effect of a portal systemic shunt and surgical repair of the biliary obstruction upon long-term survival. Baker, Jones, and Hazelrigg reported a death from esophageal hemorrhage in a patient in whom a surgical stricture of the common bile duct developed, followed by biliary cirrhosis. They stated that portal hypertension rarely accompanies biliary cirrhosis. This opinion is also held by Ellis and Holman. They reported no further

hemorrhage after performing a splenorenal shunt in a patient who had had 3 common duct reconstructions. However, that the development of portal hypertension is not rare in this type of disease is demonstrated by the report of Craig, Gellis, and Hsia. They reported a series of 49 cases of extrahepatic biliary atresia. Only 5 of these patients lived more than 1 year. Esophageal varices developed in all, and 4 of the 5 patients ultimately died of exsanguination. Sedgwick and Hume recently described the management of 12 patients with iatrogenic stricture of the extrahepatic bile ducts and portal hypertension. Seven bled from varices and were treated with a splenorenal shunt. The fact that 3 of these patients had recurrence of esophageal bleeding postoperatively may indicate the inadequacy of this type of shunt. It is recognized, however, that the construction of a portacaval anastomosis may be extremely difficult after multiple operations have been performed in the region of the portal vein. If a portacaval shunt can be established, it is the procedure of choice. This operation is followed by better decompression of the portal venous bed and a lower incidence of thrombosis of the shunt.

Apparently, portal hypertension and esophageal bleeding is not uncommon in biliary cirrhosis. The real incidence of bleeding, however, is difficult to ascertain since such widely divergent opinions are expressed in the literature reviewed. We suggest that larger series of patients with esophageal hemorrhage be accurately classified when reported. In this way, not only can the true incidence of portal hypertension in biliary cirrhosis be determined but also the effect of shunting procedures upon subsequent hepatic function can be clearly delineated.

SUMMARY

1. A brief review of biliary cirrhosis is presented.

2. A classification of biliary cirrhosis based upon etiology is suggested.

3. The case histories of 7 patients are included illustrating types and clinical patterns of biliary cirrhosis.

4. It is suggested that a careful study be made of patients with biliary cirrhosis and portal hypertension so that the effect of the reduction of portal pressure upon subsequent hepatic function can be determined.

5. The importance of inclusion of specific disease types in reports of shunting procedures is emphasized.

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EDITORIALS

THE DANGER OF BECOMING SATISFIED WITH STANDARDIZED TECHNIQUES

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THE TECHNICAL EXCELLENCE of a surgeon's art is important, for it is this quality more than any other that makes his operations safe and effective. In the period of training it is an advantage for him to master the standard techniques so that they may become the scaffolding on which his surgical philosophy is built. Yet there are dangers in perfecting techniques: the dangers of becoming overly enamored of the craftsmanship involved and of being reluctant to adopt new methods. The surgeon knows that employment of new techniques may, until they are mastered, result in a temporary increase in postoperative complications. As a result of this knowledge his operations may become overstandardized. The decision as to what operation should be performed may be made on the basis of what operation the surgeon does most expertly instead of on what operation would be best for the patient. When this happens and when a technique has become standardized too rigidly the operation may become a mere corollary to the diagnosis. In such cases the reflex centers of the surgeon have taken control. It is the hand that guides the mind.

When vagotomy combined with a shunt operation emerged from the laboratory as a physiologic means of reducing the gastric acidity of patients with duodenal ulcer, it was attacked by many of the surgeons who had skillfully standardized the technique of subtotal gastric resection. Today, the trend is toward increasing the use of vagotomy combined with shunt operations or small resections, but it has required more than 15 years for the more physiologic operations to replace the standardized technique of subtotal gastric resection. It is possible that the reluctance to accept the principle of vagotomy was based in part on the attachment of surgeons to their perfected techniques.

In the treatment of cancer, similar problems are presented. The combined abdominoperineal resection, the standard radical neck dissection, and the radical mastectomy are operations that have evolved through half a century of experience and are firmly established. Sometimes, to the resident in training, the performance of an operation such as an abdominoperineal resection becomes a symbol of surgical maturity. Too often, this symbol becomes established as a measure of surgical success. In such circumstances, the surgeon may continue to perform combined abdominoperineal resections not because the tumor is so located that sacrifice of the rectum is essential, but because by training and experience he has mastered the technique and

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has brought himself to believe that even in high-lying lesions the tumor cannot be eradicated without sacrifice of the rectum. Yet many thoughtful surgeons have found that in properly selected cases low anterior resections or pull-through operations are just as effective as operations that remove the rectum.

The block dissection for metastatic cancer of the neck is another example of the effect of standardization of technique on surgical practice. This operation, with sacrifice of the sternocleidomastoid muscle, the eleventh nerve, and often the inframandibular branch of the facial nerve, is an effective way of dealing with extensive metastases from squamous cell cancers of the mouth. The metastases of these cancers are invasive, tend to penetrate the capsules of the nodes, and often cannot be controlled satisfactorily by lesser operations. The patients requiring such dissections are mainly elderly men in whom cosmetic considerations are not important. In such cases, the standardized operation is clearly indicated.

When the standard neck dissection is applied prophylactically, in the absence of palpable nodes, and particularly when it is applied to young women with encapsulated metastases from papillary carcinomas of the thyroid, the situation is different. The deformity of the neck and the late disturbances in the function of the shoulder are highly undesirable in the younger age groups in which papillary tumors tend to occur. In operations for this type of tumor, and perhaps also in some of the prophylactic operations for squamous cell cancer, an adequate en bloc resection of the fat and lymph node-bearing tissue can be performed without sacrificing important structures. It is possible to modify the standard procedure and adapt it to these special cases.

Radical mastectomy for cancer of the breast is another standardized operation in which at times the surgeon's hands may lead his mind. Thoughtful surgeons, like Haagenson, have shown that when the apex of the axilla is involved with cancer, radical mastectomy cannot be expected to effect a cure. If such involvement can be demonstrated by biopsy of the apex of the axilla, many surgeons agree with Haagenson that radiation therapy gives better palliation than do radical operations.

Despite these frank admissions of the surgical incurability of mammary cancers that involve the apex of the axilla, many surgeons continue to perform extensive dissection of the involved apex and of the fat and the lymphatics above the axillary vessels. Often radiation therapy is added. In half of such cases, edema of the arm ensues, and in some cases the edema is a source of major morbidity. Is this another example of the danger of overstandardizing surgical techniques? When extensive involvement of the apex of the axilla is found, might it not be better to treat it by radiation? In "prophylactic" axillary dissections, when no gross involvement is evident, is it really worthwhile to carry the dissection to the apex and to dissect above the vessels with the attendant risk of causing edema of the arm? Is it necessary in every case to graft skin, to sacrifice muscles, or to place the scar in a conspicuous position? Here again it sometimes seems that the technique of the operation has become a mere corollary to the diagnosis—a ritual from which few surgeons dare to deviate.

In many fields our standard techniques should be re-evaluated in the light of modern insight into the physiology or natural history of disease. Oftentimes such re-evaluation can lead to modified or new techniques with reduction in operative morbidity. Familiarity with a technique should not have undue influence on the choice of operation. *It is the mind that should guide the hand.*

SURGICAL CONVALESCENCE

PAUL R. HAWLEY, M.D., Chicago, Illinois

WHEN SURGERY was a manual art largely confined to the correction of localized defects, a surgical operation of itself was a debilitating experience. Anesthesia was crude, often followed by serious sequelae; and metabolic imbalances resulting from improperly regulated nutrition produced real illness from which the patient had to recover as well as to convalesce from the local effects of his operation.

Little was known about the healing of wounds, and the process was generally believed to be much slower than it actually is. Fear of wound separation was a factor in delaying ambulation, but often the patient was too ill or too weak to leave his bed until after the skin sutures had been removed. The longer the patient remained in bed, the more time was required to regain strength and resume normal activities.

A pattern of prolonged convalescence from surgical operations was established in this past era; and surveys reveal that this pattern is followed today by some surgeons, despite the alleviation of most of the ill effects of surgery through better anesthesia, scientific preoperative and postoperative care, and early ambulation.

More and more surgeons are recognizing a social as well as a professional responsibility. No longer do they dismiss patients upon recovery from the immediate effects of the operation, but continue supervision until maximum possible function has been restored through rehabilitation. The data presented by Dohan, Taylor, and Moss suggest that this growing interest in the subsequent welfare of surgical patients now should be focused upon the adverse effects of unjustifiably prolonged convalescence.

That there is an economic loss, to the nation as well as to the individual, is apparent. But, perhaps of greater importance, is the possibility of a psychologic effect upon the individual of being paid, through some form of disability compensation, for doing nothing. There is some evidence which suggests that insurance benefits may act as a deterrent to return to work. Surgeons should be careful not to encourage such an abuse.

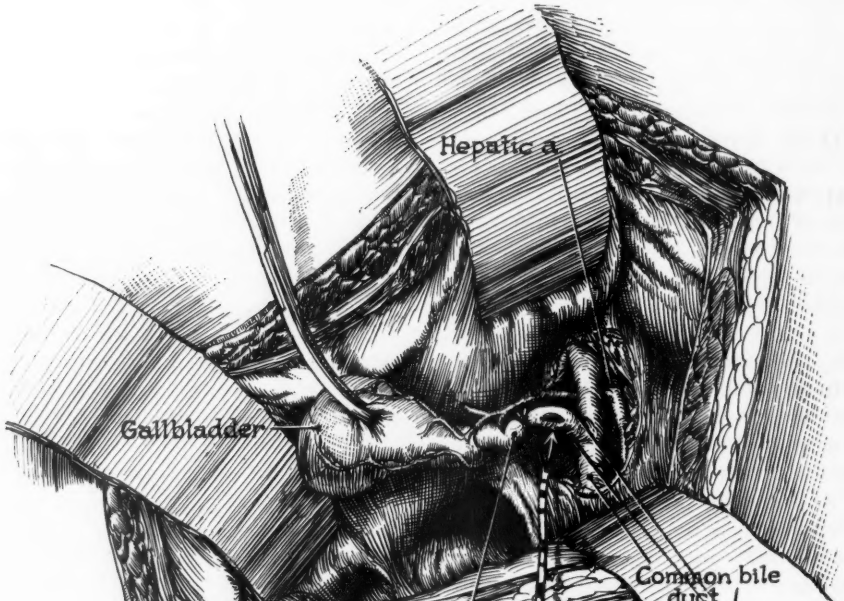


FIG. 1. Technique of operative cholangiography.

Technique and Evaluation of Operative Cholangiography.—James P. Isaacs and Marvin L. Daves.

THE SURGEON AT WORK

TECHNIQUE AND EVALUATION OF OPERATIVE CHOLANGIOGRAPHY

JAMES P. ISAACS, M.D., and MARVIN L. DAVES, M.D., Baltimore Maryland

In 1932, Mirizzi introduced operative cholangiography. Although oral cholecystography has become a mainstay in gallbladder diagnosis, operative cholangiography has never gained widespread acceptance in the United States. Reports from numerous clinics in which it has been employed have differed regarding its value.

This article emphasizes the simplicity of the equipment and technique for operative cholangiography since considerations along these lines have apparently been major deterrents to its use. Clinical observations substantiating its value as a diagnostic tool are presented. An assessment is made of: (1) the value of operative cholangiography in the detection of unsuspected common duct stones during routine cholecystectomy for gallstones, (2) its value in the detection of hepatic duct and residual common duct stones during common duct exploration, and (3) its possible value in safely avoiding common duct exploration under certain conditions. Illustrations are included to demonstrate the merit of the predissection cholangiogram—done prior to common duct dissection or exploration—the postdissection cholangiogram, and the postoperative cholangiogram and also to demonstrate the assistance of operative cholangiography with a number of more complicated types of biliary tract surgery.

EQUIPMENT

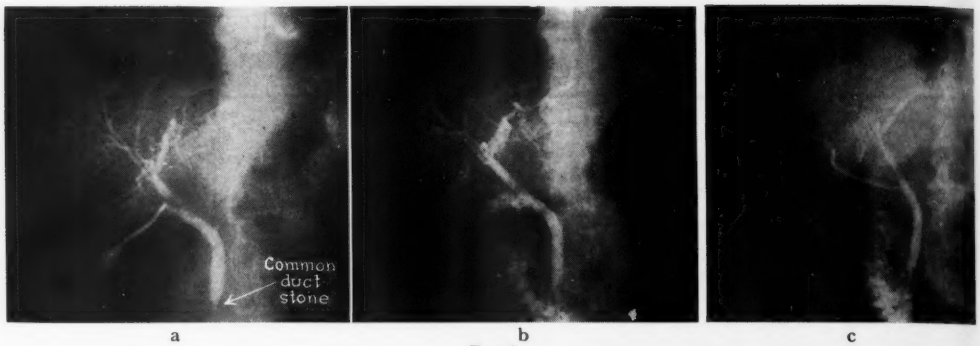
An outline for an operating room cholangiographic procedure is given using materials which are likely to be available in a general operating room area. The use of more elaborate equipment can enhance the ease of performance, but the additional expense will be out of proportion to the improvement in the quality of the results. Roentgenographic equipment should include: (1) a portable x-ray machine (50 to 300 milliamperes), (2) three 8:1 grid cassettes—10 by 12 inches or larger (3) a wooden cassette tunnel, (4) a supply of water soluble radiopaque contrast material (50 per cent hypaque), and (5) darkroom facilities for developing the films. Surgical equipment necessary is as follows: (1) a small polyethylene or No. 5 olive tipped ureteral catheter or No. 22 to 25 needle, and (2) 2 syringes, at least 1 being 20 cubic centimeters.

TECHNIQUE

The cassette tunnel should be placed between 2 pads on the surgical table beneath the patient, positioned so that the middle of the tunnel will be at the level of the xiphoid process. It is advisable to obtain a preliminary film which can be done conveniently before draping in order to check the technique. The actual factors used will depend upon the size of the patient and the available equipment, but 50 milliampere-seconds at 75 kilovolts should cover the average situation.

For the predissection cholangiogram, a syringe containing saline is adapted to the ureteral catheter using a No. 20 or 22 needle and is ready before incision. Care must be taken to eliminate all air bubbles. The surgeon dissects and ligates the cystic duct. A second ligature is placed proximally about the cystic duct and left untied. The cystic duct is then opened fairly

From the Departments of Surgery and Radiology, The Johns Hopkins Hospital, Baltimore.



a b c

FIG. 2.

FIG. 3.

a

b

FIG. 4.

FIG. 2. A 69 year old colored female. a, Predissection cholangiogram shows convex opacity at the intramural portion of the common duct. b, After common duct exploration has been carried out and the stone removed, check cholangiogram shows contrast medium going down into the common duct and no stones. c, Postoperative T-tube cholangiogram reveals excellent flow of contrast medium into the duodenum, a delicate intramural portion of the common duct, and no stones.

FIG. 3. This illustration demonstrates the critical value of diagnostic cholangiography. A 72 year old white female entered the hospital with jaundice. On thorough exploration of the common duct, including duodenotomy with exploration forward and backward through the intramural portion of the common duct, no stones could be found. A predissection cholangiogram was not done before the exploration. A T tube was placed into the common duct after the negative exploration, and a film obtained. Note left hepatic duct is cut off abruptly. A re-exploration with careful probing into the left hepatic duct produced a stone. There was mild congestive failure with some chronic passive congestion of the liver. A block of a single large hepatic duct appears capable of causing mild jaundice under such conditions.

FIG. 4. The value of quantitating and localizing the disease before a common duct exploration is shown. A 69 year old white female. a, Diagnostic cholangiogram shows the distal portion of the common duct completely obscured, and no contrast material can be seen going down into the duodenum. There is a cut off in the left hepatic duct. Eight 4 to 8 millimeter stones were removed from the common duct. A successful effort was made to remove the larger stone from the left hepatic duct. b, Check film with T tube in place after common duct exploration with filling of the left hepatic duct and contrast medium going into the duodenum. Note, also, pancreatic duct.

close to the common duct. The tip of the catheter is inserted through the cystic duct until it just enters the common bile duct. The previously placed ligature is tied to secure the catheter in an airtight fashion. A reflux of bile into the syringe on gentle aspiration or a free flow of saline into the duct without extravasation into the peritoneal space assures proper catheter positioning. The syringe is then exchanged for one containing contrast medium. All clamps and packs are removed from the wound. The incision drapes remain, and an additional sterile

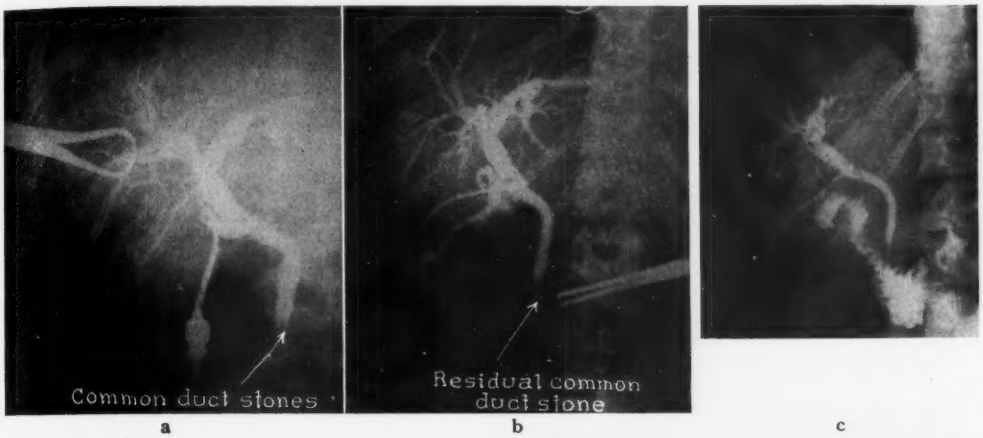


FIG. 5.

FIG. 5. Again, the value of predissection cholangiograms is demonstrated as well as the critical value of a postdissection cholangiogram. A 30 year old colored female. a, Note filling defect at the lower end of the common duct without flow into the duodenum. b, A check cholangiogram after the common duct has been explored, a stone has been removed, and a T tube is in place. Note, however, obvious stone remaining in the duct. Additional exploration was required to retrieve the residual stone. c, Postoperative T-tube cholangiogram showing delicate intramural portion of the common duct, no stones, and free flow into the duodenum.

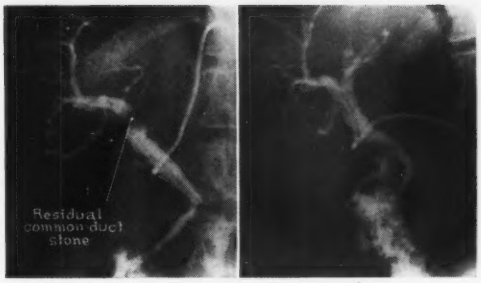


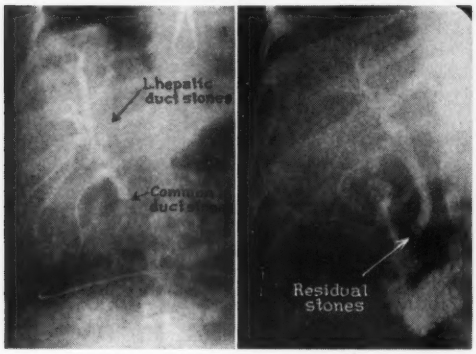
FIG. 6. a, Both the need for a postdissection and the value of a postoperative cholangiogram are dramatically demonstrated. A 59 year old white male had been jaundiced. A common duct exploration revealed stones. No operative cholangiogram was done. A T tube was introduced into the common duct. Postoperatively, the jaundice did not clear. Postoperative cholangiogram through the T tube shows a large common hepatic duct stone. Reoperation was carried out for removal of the stone. The stone is gone on check film at re-exploration.

towel is used to cover the incision. The portable x-ray tube is then centered over the incision. An x-ray tube suspension is convenient but not necessary. In the adult, 3 leisurely injections of 6, 6, and 8 cubic centimeters are made. A total of 3 diagnostic or predissection films are obtained, 1 after each injection and cassette change. The first film is a horizontal view, the second slightly left oblique, and the third right oblique. These positions are easily achieved by tilting the table to either side.

The anesthesiologist and the x-ray technician are supplied with lead aprons. Other shields or out-of-room x-ray controls may be used. After each injection and before each film is exposed, the surgeon, assistants, and nurses leave the room. The anesthesiologist then renders the patient apneic and signals the technician to take the film. The cassette tunnel makes film changing relatively simple, care being taken to avoid contaminating the drapes. Operating table models are available for making the film changes at the head of the patient, but are not essential.

The surgeon proceeds with the cholecystectomy while the films are being processed. Interpretation of the cholangiograms by a roentgenologist experienced in the roentgenographic anatomy and pathology of the biliary tree is of major importance. The time required for diagnosis should be less than 10 minutes. In cases in which common duct exploration is carried out and a catheter or T tube is left in the common bile duct, the roentgenographic procedure should be repeated. These check or postdissection films can then be processed while the surgeon is preparing to close the wound.

The ureteral catheter has proved a convenient injection device; however, in a few cases, for



a FIG. 7. b

FIG. 7. The need for both predissection and postdissection cholangiography is shown in another way in this illustration. A 27 year old colored female. a, The distal portion of the common duct is cut off. There is no filling of the left hepatic duct. Stones were found in the left hepatic duct and multiple stones removed from the common duct. A check cholangiogram was not obtained. b, Postoperative T-tube film reveals numerous stones in the lower end of the common duct. The left hepatic duct has been cleared and fills. More stones were removed from the common bile duct when the patient was again taken to the operating room.

FIG. 8. Sickle cell anemia does not usually produce symptomatic gallbladder or common duct stones. In this patient with sickle cell anemia the value of operative cholangiography in detecting unsuspected common and hepatic duct stones when doing routine cholecystectomy for gallstones is shown. A 30 year old colored female had sickle cell anemia with multiple abdominal crises, and had been admitted to the hospital 18 to 20 times. On this particular occasion, the surgical consultant believed that she had gallbladder colic. At operation the gallbladder contained bilirubin stones. The common duct looked and felt normal. a, Routine cholangiogram reveals numerous stones in the lower end of the common bile duct and several in the left hepatic duct. Twenty-three smooth, freely movable bilirubinate stones were removed from the common duct and the intrahepatic biliary system. b, Check cholangiogram indicates that 2 sizeable stones remain, 1 at the lower end of the common duct and 1 in the left hepatic duct. After these were retrieved another check cholangiogram was clear, as was the postoperative T-tube cholangiogram. Value of routine operative cholangiography and of check cholangiography is shown.

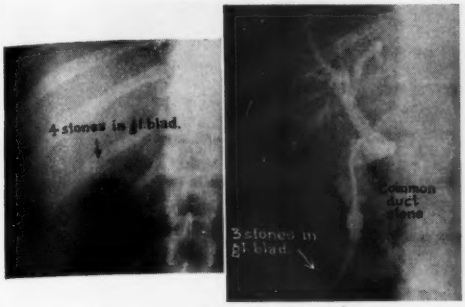
TABLE I.—CLINICAL OBSERVATIONS IN BILIARY TRACT SURGERY, JOHNS HOPKINS HOSPITAL, 1954–1959 (JANUARY)

		Operations	*Operative cholangiograms*
Cholecystectomies	681		87
Cholecystostomies	5		
		686	
Common duct explorations			53
for stones	203		
for strictures	16		
for hepatitis	4		
		223	
Common duct by-pass surgery			9
Whipple resections for cancers	39 / 4		
		43	
Sphincterotomies ± other procedures	13		6
By-pass surgery	1		
Cholecystectomy alone for chronic relapsing pancreatitis	1		
		15	
Exploratory laparotomy for acute pancreatitis		3	
Exploration porta hepatis for biliary atresia		6	1
Choledochoduodenostomy (2) / Excision of choledochal duct cyst (1) for choledochal duct cyst		3	1
Total		979	157

instance when a stricture is being located a fine needle—No. 22 to 25—may be used for direct puncture of the common bile duct.

Free flow into the duodenum is usually seen on the predissection roentgenograms before surgical manipulation of the common duct. If, before any sort of exploration or instrumentation of the common bile duct is carried out, the contrast medium does not flow into the duodenum, a stricture at the sphincteric region should be suspected. On the other hand, after common duct exploration and instrumentation of the transduodenal region, edema or spasm frequently prevents passage into the duodenum. This must be taken into account in the interpretation of the postdissection films. Postoperative cholangiograms on the eighth or tenth day show free flow in these instances. To emphasize this point, if a stone is visualized on diagnostic cholangiography and is removed, failure of free flow of contrast material into the duodenum on the postdissection cholangiogram should not unduly concern the surgeon.

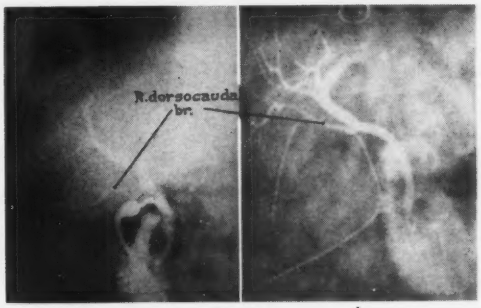
A number of investigators have made interesting suggestions regarding variations in the technique.



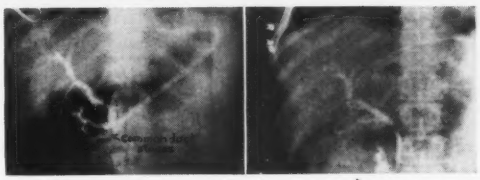
a FIG. 9. b

FIG. 9. Again, the value of routine cholangiography is demonstrated to show the possibility of actually milking sizeable stones from the gallbladder into the common duct when doing a cholecystectomy. A 28 year old white female. a, Four stones lie in a straight line in the gallbladder, on the scout film taken before surgery. The gallbladder was dissected from its bed before diagnostic cholangiograms were taken. b, Diagnostic cholangiogram shows 3 stones in the gallbladder along the catheter at the lower midportion of the film. The fourth is at the end of the common duct as a very distinct radiolucent foreign body. It was removed.

FIG. 10. Another value of operative cholangiography is the demonstration of normal bile duct anatomy and congenital bile duct anomalies. For the inexperienced surgeon this can be of immense value. a, A 52 year old white female. Routine cholangiogram made during cholecystectomy. The anomaly is at the entrance of the dorsocaudal branch of the right hepatic duct directly into the common hepatic duct, a short distance above the cystic duct. The dorsocaudal branch loops up over the right hepatic vein, goes distinctly posterior, and divides. Its approach to the common hepatic duct usually can be seen on the normal cholangiogram situated between the left hepatic duct and the ventrocranial division of the right hepatic duct. b, A 52 year old colored female. The dorsocaudal branch of the right hepatic duct joins the cystic duct and together they enter the common bile duct, one of the most common anomalies of importance in biliary tract surgery.



a FIG. 10. b



a FIG. 11. b

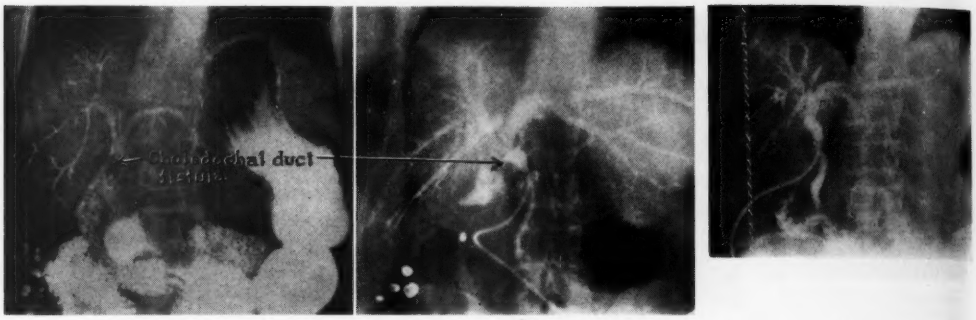
FIG. 11. At times an operative cholangiogram may save a common duct exploration, for instance, in the patient with a questionable history of jaundice, in a patient who has been operated upon inadvertently with pancreatitis or hepatitis, or in a case like the one demonstrated in this figure. A 72 year old colored male was jaundiced and had a hypotensive episode with anesthesia. Blood pressure rose somewhat after induction. Since it was thought that there was definitely common duct obstruction, the procedure was undertaken. Numerous stones were found in the gallbladder. While the common duct was being palpated, the patient had another hypotensive episode. A small catheter was quickly threaded into the cystic duct, a cholangiogram obtained, the gallbladder removed, and the incision was closed within 10 minutes; the patient recovered. a, A series of small stones at the lower end of the common bile duct (1 to 3 millimeters in size) may be seen. b, Two weeks later the common duct was completely free of stones and there was good flow of contrast medium into the duodenum. Jaundice subsided.

CLINICAL OBSERVATIONS

Table I summarizes 979 cases, the total experience in biliary tract surgery at The Johns Hopkins Hospital between January 1954 and January 1959.

Staff and resident surgeons were equally represented. Eighty-seven routine cholecystectomies were accompanied by operative cholangiography. In 585 similar cases, operative cholangiography was not performed. In these, operations were carried out for cholecystitis and cholelithiasis. Common duct explorations for stones were carried out in 203 instances. In 49 of these operative cholangiography was done. Fifty-seven of these patients did not have operative but did have postoperative cholangiograms.

In the 87 routine cholecystectomies for gallstones, unsuspected stones were discovered in the common duct by operative cholangiograms in 7 patients (8.0 per cent). Congenital duct anomalies of surgical significance were observed in 3 patients (3.4 per cent). At a rate of 8.0 per cent, unsuspected common duct stones would be expected in 47 of the 585 patients operated upon without roentgenograms. The unsuspected milking of a large sized stone from the gallbladder into the common bile duct during surgical manipulation was also demonstrated.



a b c

FIG. 12. A 71 year old white female. a, Gastrointestinal series shows barium actually passing through a choledochoduodenal fistula from the second portion of the duodenum upward into the common hepatic duct at a point where the hepatic ducts join. Barium has gone into the radicals of the left and right hepatic ducts. b, At surgery, operative cholangiogram made through the cystic duct shows contrast medium going from the junction of the hepatic ducts downward into the second portion of the duodenum. It also passes down the common bile duct. c, The fistula was closed; postoperative film shows filling of biliary tree without passage of contrast medium into second portion of duodenum. It passes normally from the common bile duct into the duodenum.

Common duct explorations for stones were done without operative cholangiography in 150 patients with a positive yield of stones in 57 (38 per cent.) Common duct explorations for stones, performed with operative cholangiograms, in 49 patients yielded stones in 24 (49 per cent) instances. Specifically, however, 24 positive cholangiograms were borne out by the finding of stones on exploration in 23 (95.8 per cent) of these patients; 25 negative cholangiograms were accompanied by the finding of no stones on exploration in 24 (96 per cent) of these patients. Thus, the accuracy of operative cholangiography in all 49 cases was 96 per cent.

Hepatic duct stones were visualized by operative cholangiography in 6 of 49 patients having common duct explorations (12.5 per cent). Of the 24 patients actually discovered to have stones, 6 had hepatic duct stones (25 per cent).

Residual common duct stones were revealed by postoperative cholangiograms in 6 of 57 patients (10.5 per cent) in whom common duct stones had been removed without the aid of operative cholangiograms. Residual common duct stones were seen in postoperative cholangiograms in none of 24 patients in whom common duct stones had been removed with the benefit of operative cholangiography. In 3 of these patients (12.5 per cent) residual common duct stones would not have been found if a check cholangiogram had not been taken.

Of 150 common duct explorations without operative cholangiography, 9 (6.7 per cent) could have reasonably been avoided by the use of cholangiograms. Of 87 routine cholecystectomies with operative cholangiography 15 common duct explorations were avoided by the use of the x-ray study (17.2 per cent). In these patients, the history of jaundice was indefinite or the patient had subacute gallbladder inflammation with mild chemical jaundice which promptly disappeared after operation and has not reappeared after at least a 2 year follow-up period. Also, in these cases the operative cholangiograms were of good quality, and interpretation was not equivocal, an obvious requisite.

Of a total of 157 operative cholangiograms for all types of disease, 6 of the studies (3.8 per cent) were of poor quality or technically unsatisfactory because of positioning, respiratory motion during x-ray filming, overlying surgical instruments, failure to inject the contrast medium into the biliary tree, or passage of the injecting catheter into the duodenum. In almost every case these were associated with the initial development of the technique of the procedure, or the early experience of the particular surgeon, or the severity of the pathologic condition. There was 1 false positive and 1 false negative in 49 common duct explorations accompanied by operative cholangiography (4.1 per cent).

DISCUSSION

The incidence of unsuspected common duct stones during routine cholecystectomy for gallstones has been reported to be from 6 to 26 per

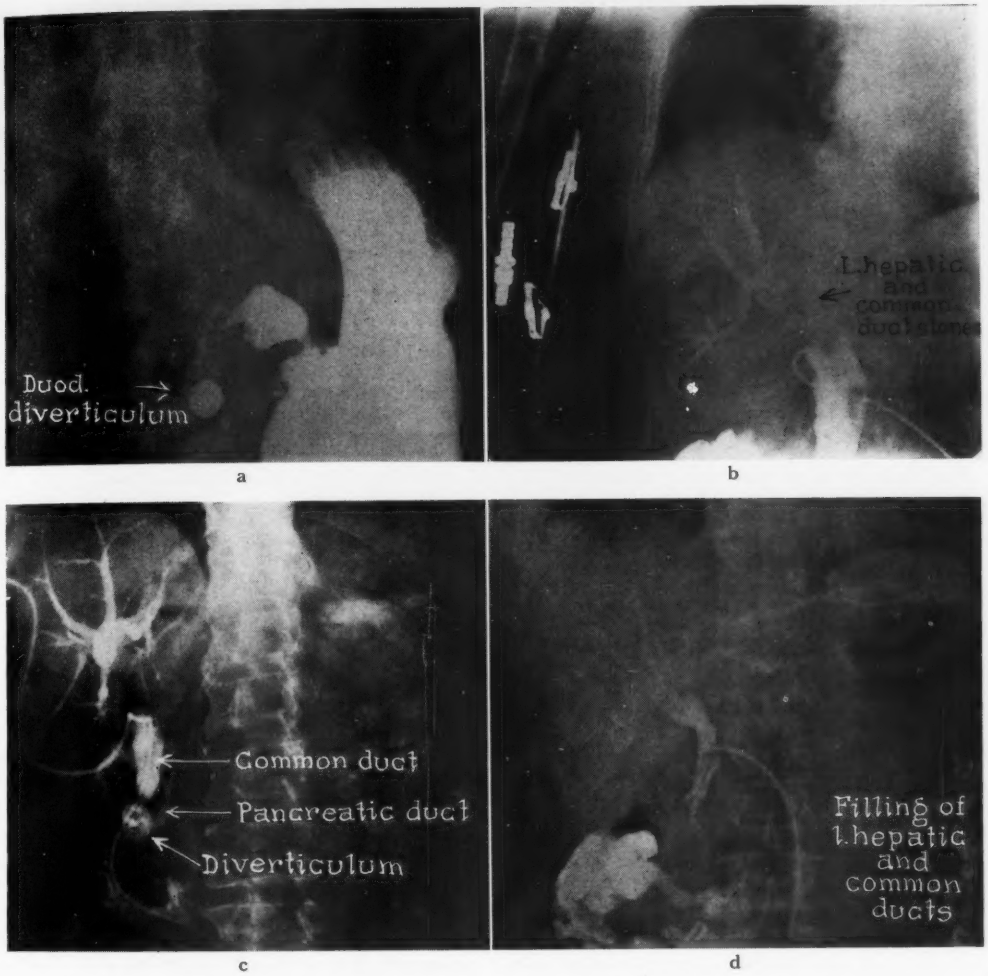
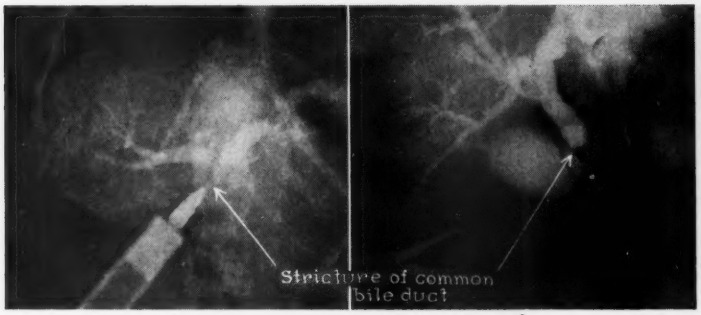


FIG. 13. A 72 year old white female. a, Gastrointestinal series of this jaundiced patient reveals a diverticulum in the duodenum. b, At surgery, a diagnostic cholangiogram was obtained which shows numerous large stones in the greatly dilated common bile duct. Note numerous stones in common hepatic duct and that left hepatic duct does not show. c, Left hepatic and common ducts are well filled after extraction of many large stones. The contrast medium has traversed the common bile duct into the diverticulum which receives the pancreatic duct separately. d, Check cholangiogram shows good filling of left hepatic duct and no stones in biliary tree.

cent. The experience in this report falls at the lower end of this spectrum (8.0 per cent) and correlates well with Glenn's report on 100 patients who had routine cholecystectomies and were followed up for 10 years. Seven per cent required re-exploration because of symptoms and 4 per cent had stones on common duct exploration.

The incidence of intrahepatic duct stones visualized on operative cholangiograms during 195 common duct explorations which were positive for stones was 24 per cent in Norman's series. The figure from this report is 25 per cent.

The incidence of residual common duct stones after common duct exploration has been reported variously between 2 and 26 per cent. Residual stones with and without operative cholangiography checked by postoperative cho-

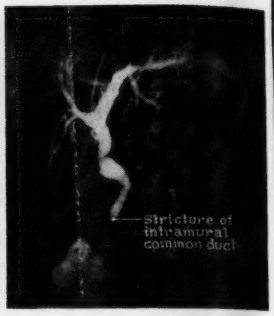


a

FIG. 14.

FIG. 14. A 26 year old white female. By injecting opaque medium directly through a No. 22 or 25 needle, cholangiograms can be obtained anywhere along the biliary tract. a, This patient had had a cholecystectomy 6 months earlier. At exploration for jaundice the porta hepatis was heavily scarred. From the needle cholangiogram it is obvious that there is a stricture just beyond the junction of the hepatic ducts. b, A 54 year old white male. Postcholecystectomy common duct stricture is well visualized which aided in dissection for end-to-end repair.

FIG. 15. A 26 year old white female. Predissection cholangiography assisted in solving a difficult problem. A cholecystectomy had been performed at age 22 for gallstones. Almost immediately postoperatively and at increasingly frequent intervals for 4 years there was right upper quadrant pain with gaseousness and vomiting causing severe incapacitation. Intravenous cholangiograms showed a slight enlargement of the common duct which suggested distal common duct obstruction. There was never any jaundice. The pancreas, stomach, and duodenum were normal. The cystic duct remnant was fairly large but contained no stones. Operative cholangiogram shows constriction at the lower end of the common duct with no flow of contrast medium into the duodenum. On common duct exploration, a probe could not be passed through the ampullary region. Duodenotomy was performed, and a stricture at the sphincter was detected. A sphincterotomy was performed. Biopsy indicated no tumor. The diagnosis was stenosing papillitis. Pain was relieved.



b

FIG. 15.

langiograms in the present series totaled 0 and 10.5 per cent respectively. The latter figure, without operative cholangiograms compares with 8 per cent of 153 cases according to Johnson and associates, 9.7 per cent of 54 cases of Glenn, 8 per cent of 190 cases of Buxton and Burke, and 12 per cent of Hicken and coworkers.

Residual common duct stones have been reported to cause gastrointestinal symptoms in 70 to 85 per cent of the cases, to produce jaundice in 20 to 40 per cent, and to necessitate surgical re-exploration in 35 to 70 per cent. In our series in which 6 patients had cholangiogram-proved residual common duct stones, the percentages were 83.3 per cent symptoms, 50 per cent jaundice, and 83.3 per cent re-exploration.

The size of a stone which will obstruct the common bile duct and probably not spontaneously pass the sphincter of Oddi has been estimated at 5 millimeters or larger. In the present series the stones visualized and later removed measured 5 millimeters or more in 5 of 5 patients. This value is somewhat variable since a 2 to 3 millimeter cholesterol stone within an inflamed intramural position of the common duct is known to be capable of causing obstruction. On the other hand, Figure 11a shows a number of 2 to 3 millimeter stones which later passed through the sphincter of the common duct. It appears wise in cases of residual common duct stones smaller than 5 millimeters to allow several weeks for passage before re-exploration. In agreement with Glenn, however, a stone definitely visualized upon postoperative cholangiography should not be permitted to remain in the common duct without re-exploration or T-tube x-ray follow-up examination.

The subject of operative cholangiography always raises the question of toxicity or morbidity. The unavoidable morbidity associated with common duct disease and allied surgical operations makes morbidity secondary to cholangiography difficult to assess accurately. In the present group of 87 cholangiograms performed at the time of routine cholecystectomy, there were no untoward effects. The postoperative courses were not unusual. In 300 patients in Sherman and Stabins' series, there was no morbidity with operative cholangiography. In 8 patients in a series in which 460 operative cholangiograms were made, Rigler and Mixer

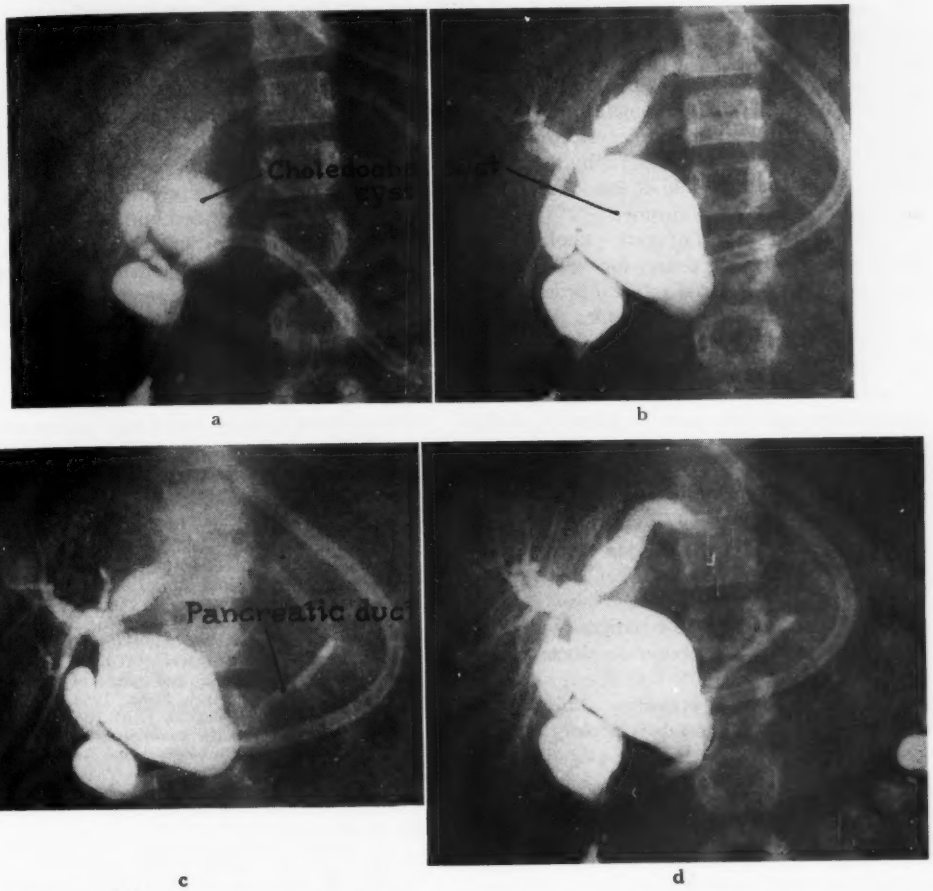


FIG. 16. Composite of 4 cholangiograms reveals needle injection into a choledochal duct cyst. As the medium is injected in progressive illustrations, the common duct cyst gets bigger and in the third illustration the pancreatic duct visualizes. In the fourth, distal common duct shows for the first time. In addition, small radicals of the pancreatic duct are now seen. Treatment was anastomosis between duodenum and common duct, side-to-side.

obtained pyelograms, meaning that contrast medium entered the blood stream. These occurred with common duct obstruction. In 153 cholangiograms in the present group, pyelograms were obtained twice. The significance of this observation is not known, but it is to be recalled that these same agents are injected intravenously daily into many patients for pyelography. The pancreatic duct was visualized without complication in 25 per cent of the 225 cases in Brown and Brown's series. Swedberg reported a similar experience in 21 per cent of 700 patients. The development of pancreatitis after pancreatic duct visualization may occur but has never proved serious. Contraindications to operative cholangiography are few. The principal situation in which discretion must be used is in severe, acute inflammatory disease when only minimal biliary dissection and exploration are advisable.

SUMMARY

1. A consideration of the equipment, technique, and clinical value of operative cholangiography is presented. Results with 979 biliary tract procedures and 157 operative cholangiograms are reported.

2. Eighty-seven cholangiograms were carried

out during routine cholecystectomy for gallstones. Unsuspected common duct stones were found in 7 patients (8.0 per cent) and congenital bile duct anomalies in 3 (3.4 per cent).

3. Inadvertent milking of gallstones into the common duct during cholecystectomy was demonstrated by cholangiography on 3 occasions. This could be one of the sources of the postcholecystectomy syndrome.

4. The routine use of operative cholangiography with cholecystectomy for gallstones is recommended as optimal surgical practice.

5. Residual common duct stones were noted on the postoperative cholangiograms in 6 of 57 patients (10.5 per cent) who had had positive common duct explorations without operative cholangiograms. Of these 6 patients, 5 had symptoms, 3 had jaundice, and 5 had re-exploration because of residual stones. Of 24 patients with common duct stones who had predissection and postdissection cholangiograms, none had residual stones upon postoperative cholangiography.

6. Hepatic duct stones were visualized by cholangiograms in 6 of 24 patients who were found to have stones on common duct exploration.

7. The accuracy of operative cholangiography, checked by common duct exploration, was 96 per cent in both the presence and absence of stones.

8. The yield of stones from common duct exploration when cholangiography was performed was 11 per cent higher than when cholangiography was not undertaken.

9. Three figures from different groups of patients which show a striking correlation in this study are: 10.5 per cent residual common duct stones in positive explorations without operative cholangiography, 12.5 per cent common duct stones which would have been missed but were removed at surgery because of check postexploratory cholangiography, and 11 per cent additional yield of stones from common duct explorations performed with operative cholangiography.

10. Because of this approximate and avoidable 10 per cent surgical error, operative cholangiograms are recommended with all common duct explorations, diagnostic before exploration and especially check after exploration.

11. Operative cholangiograms are more rapidly accomplished, accurately interpreted, and helpful to the surgeon when they are executed frequently or as a routine. About 10 cases are required to gain the teamwork necessary to obtain films quickly and easily and to develop satisfactory interpretative skill.

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A NEW DEVICE FOR THE MANAGEMENT OF THE TRANSVERSE COLOSTOMY

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GENERAL SURGEONS concerned with the pathology of the gastrointestinal tract are aware of the significant occurrence of complications of colonic diverticulitis requiring the creation of a proximal transverse colostomy as the first of 3 surgical procedures for the adequate control of the disease. Perforation with formation of abscess and peritonitis, the development of sigmoidovesicle fistulas in males and of pelvic masses in females, and acute obstruction in chronic stenosing diverticulitis, almost without exception, require transverse colonic diversion along with drainage when applicable. This is true, also, in cases of acutely obstructing carcinoma of the tubular more distal colon. In years past, discussion centered more upon the type of colostomy to be created, i.e., loop colostomy, the Lahey double-barrelled spur, or the Devine colostomy, than on measures aimed at the control and collection of the proximal colonic fecal discharge.

In contrast to the sigmoid colostomy, when satisfactory control may be developed, the diverting transverse colostomy is difficult to manage and creates, in some instances, serious emotional, social, and economic problems. Since a defunctionalizing transverse colostomy is performed with sufficient frequency for both inflammatory and malignant disease, for periods of 4 to 12 months with the former, and of 1 to 3 months with the latter, the physical and psychologic well-being of the patient demands recognition. The need for a satisfactory collecting device has universally been appreciated. Such a device has been designed by a patient who came under our care. Subsequently, it was used in a clinically significant group of patients under our supervision with general satisfaction.

It has been possible to observe closely 34 patients with surgical diverticulitis treated at the Albany Hospital from June 1955 to June 1959 who required a temporary transverse colostomy. From them, the following information has been gleaned: (1) All patients reported that bowel movements were unpredictable. (2) Twenty-nine reported movements to be loose and diarrheal in character; only 5 indicated formation of solid stools. (3) All patients reported evacuations usually after each meal, during sleeping hours, and irregularly throughout the day. (4) All patients required the use of a collecting device.

This intractable behavior of the transverse colostomy is common knowledge, and the causes are as follows: (1) The right half of the colon does not remove enough water from the stool and shows little tendency to take over this function even after 3 to 6 months. (2) Persistent disease in the pelvic colon creates increased irritability of the proximal bowel just as in ulcerative colitis treated by ileostomy. Perhaps some degree of predictable control of evacuations from the transverse colostomy might be obtained with strict attention given to diet and regular irrigations after a considerable period of time and of individual experimentation. Since most transverse colostomies are surgically closed within 3 to 6 months of their creation, any reasonable degree of control of colostomies would be effective for so short a period before it was time to close the colostomy as to make the effort at dietary and irrigational control not worthwhile. The patient's insecurity and limitation of range of activity with its consequent psychologic stress and delay in recuperation between operations has brought disfavor upon efforts at transverse colostomy control.

The emotional stress natural to the patient who requires a transverse colostomy, even for a relatively short period of time, has been distressing. The need for the patient having had a transverse colostomy to return to a normal social and economic life as rapidly as his convalescence will allow has been obvious to everyone. In the

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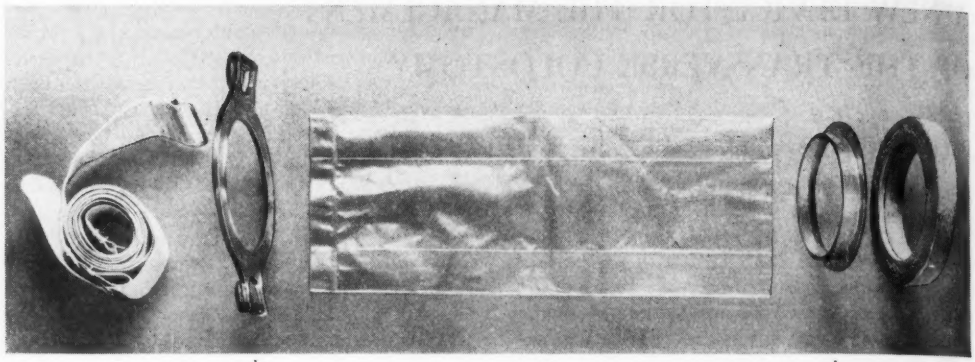

FIG. 1. Colostomy unit. a, Belt; b, lock ring; c, plastic bag; d, sponge support; e, sponge.

past, the lack of an adequate method for the collection of fecal discharge has been a handicap to the patient.

To our knowledge, a collection device designed specifically for use after a transverse colostomy has not hitherto been created. Patients sent home from the hospital with a defunctionalizing proximal colostomy to await definitive resection and subsequent closure of the colostomy have found the bags heretofore available unsatisfactory. Embarrassment and a sense of insecurity from leakage have caused confinement of many who could otherwise have returned to their normal duties.

The colostomy unit designed by a patient under our care consists of 5 parts when assembled (Fig. 1). The elastic belt slips onto hooks on either side of a lock ring. A sponge support with a circular flange is made to fit within the lock ring on the inner or body side. A soft sponge-rubber cushion grooved circularly on its inner aspect fits over the flange on the sponge support. With the sponge-rubber ring mounted on its support, a plastic bag is inserted inside of this assembly with the closed end of the plastic bag away from the exposed surface of the sponge ring. The open end of the bag is then folded back over the rubber-sponge ring for a distance of approximately 1 inch. The plastic collar or lock ring is then mounted as shown in Figure 2 by passing it over the closed end of the bag until it is seated upon the ring supporting the sponge-rubber which also includes that portion of the bag folded back in order to hold it in place. The unit is then placed over the transverse colostomy, whether this be the ordinary loop or double-barrelled type, and is held in place by the supporting elastic belt. The belt must be kept snug enough to hold the sponge-rubber ring, which conforms to the contour of the upper abdominal wall, against the skin. The plastic bag folded back over the sponge-rubber cushion and its supporting ring, held in place by the lock ring, avoids soiling; and when the belt tension is proper, slipping or shifting of the unit is prevented and leakage is avoided under the contour-fitting sponge-rubber cushion. To discard a soiled bag, the belt is unloosened, the lock ring is removed, the open end of the bag is folded back over the sponge-rubber unit, and then pulled through it and discarded. The unit is manufactured with 2 sponge-rubber ring cushions and 50 plastic bags, in addition to the lock ring, supportive rubber-cushion ring, and elastic belt. Figure 3 shows the unit mounted in the right upper abdominal quadrant on a mannequin. The unit is light weight, durable, relatively flat and inconspicuous, readily assembled, easily cleaned, and comfortable to wear.

RESULTS

Thirty-four patients who required a proximal transverse colostomy as the first of 3 operations for the surgical complications of diverticulitis of the left half of the colon were sent a questionnaire after the completion of the third stage. One patient could not be reached and was lost to follow-up. The remaining 33 patients ranged in age from 41 to 83 years. There were 22 females and 11 males. The physical status of this group

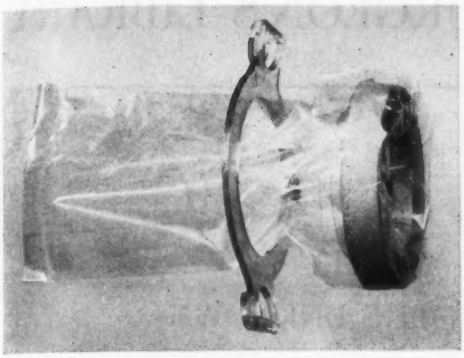

Fig. 2.

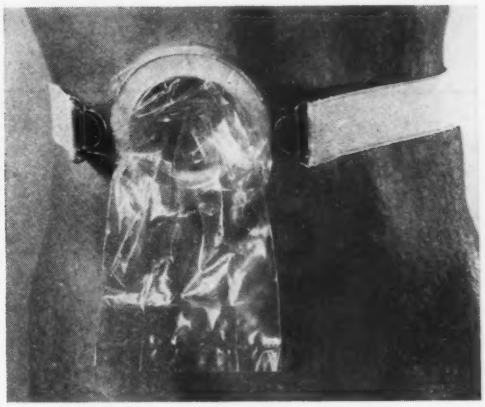

Fig. 3.

FIG. 2. Method of assembling colostomy unit.
FIG. 3. Colostomy unit mounted on mannequin.

varied, as would be expected, from the more unusual tall, thin, muscular individual with a narrow costal margin to the obese sedentary type.

In answer to the question: "Did you find the colostomy unit satisfactory?" 31 replied yes and 2 were undecided. One of these 2 patients, an obese male, had had a right rectus exploratory incision with the finding of an acute diffuse purulent peritonitis caused by perforation in acute diverticulitis of the sigmoid colon. A loop colostomy had been drawn through a right upper quadrant transverse stab wound. A large ventral hernia developed in the right rectus scar, and, by lifting up the collecting unit even though the belt was kept snug, this hernia allowed for some, though controllable, leakage. The second of these patients, a thinner woman, had an old, right lower rectus scar. This scar was depressed and extended up under the lower portion of the colostomy unit. It allowed some leakage which was controlled by inserting a piece of paper tissue or gauze under the bag at the scar site.

Those patients who had worn any other colostomy bag before acquiring this unit were the most enthusiastic about the improved features. Whereas, it would be universally agreed that no mechanical device can be a perfect answer for control of the exteriorized colon and that nothing is superior to bowel continuity, we believe that this unit is the best yet devised for the temporary proximal transverse colostomy required in the three stage operative management of certain surgical complications of colonic diverticulitis. The key to its success is the sponge-rubber cushion which prevents slipping and sliding, because of the extreme compressibility of the rubber employed. By absorbing motions of the body during the day and night and thereby overcoming accidental fecal leakage, this device has given security to those patients who have had it available to wear.

The Book Shelf

ADRENALECTOMY—A SAGA OF THE UNKNOWN

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THE SUPRARENAL GLANDS, more lately called the adrenal glands, which have been demonstrated to be so important to the existence of human life were not recognized by the ancient anatomists of Greece, Rome, and Arabia. Some authors once believed that the adrenals were mentioned in the Bible, in Leviticus, chapter 3, but the historian, Blanchard, pointed out that this was due to faulty translation of the Vulgate of St. Jerome, for many years the official Roman Catholic version of the Bible. It remained for the Renaissance anatomist, Bartholomaeus Eustachius Sanctoseverinatus, professor in the Collegia della Sapienza in Rome, to describe them first in 1563 in his *Opuscula Anatomica Venetiis* (Fig. 1). A free translation of a passage from chapter 6 of this volume relates his discovery (Fig. 2):

I judged it agreeable in this place to write on certain glands of the kidneys negligently passed over by other anatomists. For, in the upper part of the kidney (which is near the vena cava) these glandulae cling, but their outer membrane, which is continued on to the peritoneum of the diaphragm, is so bound that not infrequently unless one watches closely, when the kidneys are torn away, one passes over it as it clings tightly to the midriff. Its substance and its shape scarcely agree with those of the kidneys; although often depressed it may be so broad that it would seem rather to belong to the placenta than to the kidneys; its length is two fingers wide, and its thickness, medium. Although its dimensions are not always so, its shape does not seem to vary the least; besides, either of these glands does not have an equal size, nor keep it constantly, but in turn, now this, now that, is larger than the other; as also the kidneys near which they reside may be by turns, one greater than the other. Still it often happens that the right, as in the kidneys, is larger than the left.

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Eustachius chastised his colleagues in anatomy for their previous omission by stating:

This kind of gland should not have been passed over by former anatomists nor by those who today cultivate this art and who have written so full a treatise of human parts; especially, in following up the mistakes of others, they should show themselves so accurate and observe them so closely that they should seem to be, not contentious, but zealous for anatomical truth.

As with many other noteworthy discoveries, interest in the glandules, or renal capsules of Eustachius as they came to be called, returned to obscurity as the great anatomists of the seventeenth and eighteenth centuries—Vesalius, Fallopius, Fabricius—neglected them entirely in their writings. The idea did not die completely, however, for many of the lesser known workers heeded Eustachius' proclamation and approached the subject with a varied group of proposed physiologic attributes during the succeeding centuries.

In 1716 the Academy of Sciences at Bordeaux sponsored a prize for an answer to the question, "What is the use of the suprarenal glands?" The chief judge was the learned Montesquieu who wrote a lengthy and philosophic document to render his decision. He analyzed the many confusing and bizarre entries and finally came to the conclusion that he could find no satisfactory reply to the contest query. He summarized his findings with, "Le hazard fera peut-être quelque jour ce que tous les soins n'ont pu faire."

The eighteenth century was one of accom-

BARTHOLOMAEI
EVSTACHII

SANCTOSEVERINATIS MEDICI
AC PHILOSOPHI
OPVSCVLA ANATOMICA.

Quorum numerum & argumenta auersa pagina indicabit.

Cum Priuilegijs Summi Pont. Illustriſſ. Senatus Veneti, Serenisſ. Francorum Regis, & Catolicæ ac Cæsareæ Maiestatis.

VENETIIS,
M D LXIII.
Vincentius Luchinus excude

FIG. 1. Title page of Eustachius' *Opuscula Anatomica Venetiis*, 1563. This was the first description of the adrenal glands.

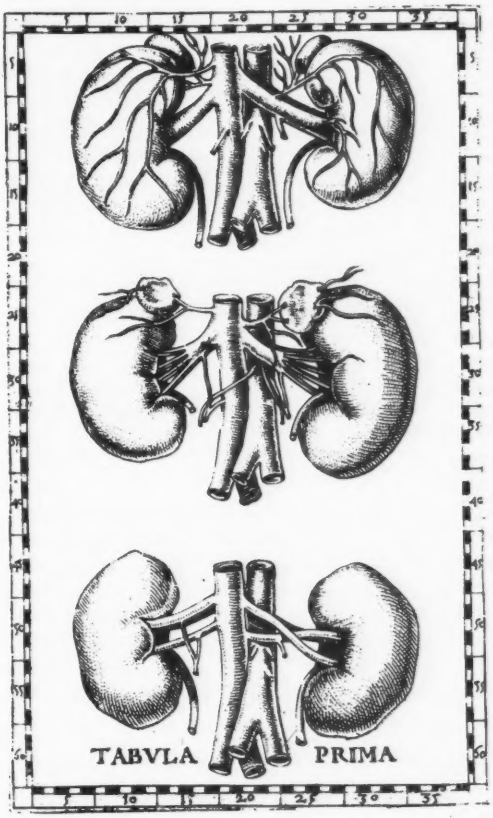


FIG. 2. Engraving which appeared in Eustachius' *Opuscula Anatomica Venetiis* demonstrating the anatomy of the adrenals.

plishment. Many names appear on the dissertations on the anatomy and function of the suprarenal glands—among them, Morgagni, Cowper, and Heister who further dissected, probed, postulated. It remained for Winslow, in 1752, to title the structures suprarenal glands and to describe most completely their gross human anatomy. Comparative anatomic studies were launched in the early 1800's by J. F. Meckel, and invaluable contributions were made by him. He was probably the first to note a possible relation between glandular activity and metabolic processes. Microscopic examination and a detailed description of the structure of the glands were the work of Ecker in 1846. The function of the glands remained obscure, however.

The turning point in the development of our knowledge of the adrenals came in 1855 when Thomas Addison published his now famous anatomicopathologic work, *On the Constitutional and Local Effects of Disease of the Suprarenal Capsule.* This was the first time that malfunction of the adrenals had been linked to human disease and marked the beginning of an appreciation of the importance of the glands for maintenance of life. Research into the entire subject, which had regressed into the doldrums, was reawakened, and 1 year later Brown-Séquard published his work in animal extirpative technique (Fig. 3). The first adrenalectomy had been performed.

Brown-Séquard, from his work, believed that the suprarenal glands were absolutely essential for life. He said, "Suppression of their function is more rapidly mortal than suppression of uri-

nary secretion." Others became interested in the possibilities offered by adrenalectomy for study of the problem of Addison's disease, and numerous publications appeared. Some refuted Brown-Séquard; others corroborated his views. Surgical shock, peritonitis, hepatitis, and nephritis were cited by his critics as the more probable causes of death in his animals, rather than some lack of an inherent property of the suprarenal glands themselves.

Brown-Séquard was prompted to work further and published a second report in which he refuted his critics and said:

> La mort à la suite de l'ablation des capsules surrénales ne peut-être attributée ni exclusivement ni principalement aux lésions qui accompagnent nécessairement ou accidentellement l'exécution de cette opération. Les fonctions des capsules surrénales sont essentielles à la vie.

The full significance of this statement was not appreciated, however, and many expositions were published to demonstrate that survival was possible in many animals after total adrenal excision had been accomplished. The presence of accessory adrenal glands was demonstrated some time later, and, of course, in retrospect, it is recognized that it was this aberrant functioning tissue which allowed survival of the animals.

Very little new was added to knowledge of adrenal function during the remaining years of the nineteenth century. Postmortem examinations of humans during that period became a very prominent part of medical teaching, and attention was called many times to tumefactions of the adrenal glands whose role in previous clinical states could not be assessed because of lack of knowledge of adrenal function. Clinical diagnosis of adrenal tumors was impossible and, hence, operative intervention was unknown. Some nephrectomies had been performed for various reasons and a few patients had survived.

It was in the autumn of 1888 that the London surgeon, J. Knowsley Thornton, received the following letter from a physician named Black, of Halifax, Nova Scotia:

> You may remember my mentioning to you during my visits to the Samaritan Hospital this summer the case of a patient of mine at the time in London, who was pronounced to have splenic tumour or enlarged spleen. She was being treated by applications of electricity, with supposed benefit. She came back here, and on my return last month I found the growth had increased materially. I have been making the electrical applications again, but the increase continues, and the discomfort is decidedly aggravated of late. She is a woman of wonderful nerve and pluck, and insists now on having a removal of this mass attempted, if any hope at all of success can be held out. I suggested her seeing you with that end in view.

The woman came to see Thornton in April 1889, and he "came to the conclusion that the tumour was not splenic, but renal, and that it could be removed, though the risk would be great." As he stated in a report to the Clinical Society of London in March 1890:

> My reasons for concluding that the case was renal rather than splenic were that all the symptoms usually associated with such an enlargement of the spleen were absent, and that the physical signs, on examining the abdomen, were those characteristic of renal tumour, the inner border of the tumour being encircled by resonant intestine, which could not be separated from it, but could on manipulation be made to contract into a raised ridge on the surface of the tumour.

He further stated that the usually well defined edge of splenic tumors which he had previously seen was absent and in addition the mass was lobulated. He apparently was able to use his hands quite accurately in palpating the abdomen and, as was proved later at operation, his original impressions were indeed correct. He goes on further to point out that the patient, who was a "married lady of 36," was "covered all over with long silky black hair, and had to shave her face just like a hairy man." It is obvious that Thornton was dealing with a functioning adrenocortical tumor. Thus, the first recorded successful adrenalectomy in a human was performed and is vividly described in Thornton's report to the Society:

> On April 11 [1889] Mr. Murray administered chloroform, and, assisted by Mr. Malcolm, I removed the tumour, using Langenbüch's lateral incision. The vessels in the mesentery and the renal vessels, which also supplied the tumour, were the largest I had ever seen in any abdominal operation. The spleen was normal, but slightly adherent to the posterior part of the tumour; the pancreas was very closely adherent and the large vessels on its surface after separation were very difficult to secure. I was obliged to pass a fine needle into the substance of the gland, carrying a thin silk ligature, in three separate places. The renal vein was quite as big as an ordinary vena cava. The tumour might quite well have been peeled away from the kidney and this organ left behind, had it not been for the renal vessels being so enormously enlarged and supplying the tumour.

The operative procedure was done at the hotel where the woman was living, for as Mr. Thornton stated:

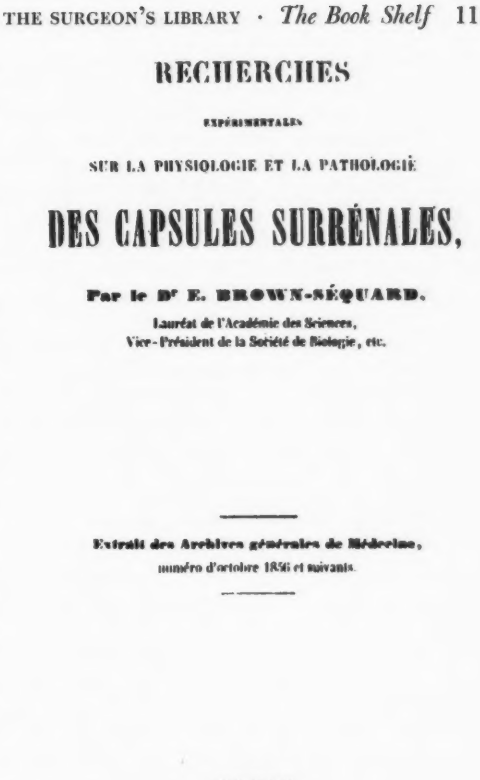
The lodging house people had not proper weights for weighing so large a mass . . . I should say this one weighed fully 20 lbs. I drained the lower pouch with a Keith's glass tube, but practically there was no oozing, and I removed the tube in twenty-four hours.

The immediate postoperative course was moderately stormy with a febrile reaction and apparently some atelectasis. A cough developed at the end of 4 weeks accompanied by high fever, and decreased movement of the left chest was noted. During a sudden fit of severe coughing the woman "felt something give way in the left side" and she coughed up a large amount of pus. It became evident then that a postoperative subdiaphragmatic abscess had drained spontaneously through the diaphragm and left lung. Recovery was prompt, and by 5 months after operation the patient stated, "I am much like my old self, and have all the external appearances of other women."

Other surgeons of the era lacked the initiative of Thornton, however, and by 1927 only 4 additional successful adrenalectomies had been reported, all for tumor. Adrenal insufficiency was probably the cause of death in most of the few unsuccessful operations attempted. Depression of function of the other adrenal by the usually functioning tumor made for inadequate hormone production to maintain life after excision of the tumor.

In 1930, the first crude adrenocortical extract was prepared; at last the proof of the vital endocrine function of the adrenal cortex had been obtained; and a new era in therapeutics was opened. Further understanding of the complex nature of adrenal abnormalities, especially tumors, was rapidly obtained, and elective operative intervention became more common as better hormone extracts were developed for replacement therapy. Great progress in understanding adrenal medullary function came at the turn of the twentieth century as adrenin was identified and isolated.

The surgical approach to the adrenal glands has taken many devious routes during the modern surgical era. The great number of pathways proposed, developed, and used clinically bespeaks the dissatisfaction of surgeons with previously described techniques available for excision of the adrenals. An early approach utilized clinically in a large number of patients was via the chest, according to Broster and Vines. Some difficulty was encountered with exposure but more important was the violation of the pleural cavity with all its complications after operation. A bilateral procedure obviously could be carried out at a single operation only with difficulty. The technique was modified somewhat later by fracturing the twelfth rib at its neck and retracting it upward with the diaphragm in attempts to improve the access to the gland. A short time later Crile proposed a modified lateral kidney incision for denervation of the adrenals as treatment for neurocirculatory asthenia. The anterior subcostal or oblique subcostal transperitoneal route was employed by Cahill and his associates for simultaneous



RECHERCHES

EXPÉRIMENTALES

SUR LA PHYSIOLOGIE ET LA PATHOLOGIE

DES CAPSULES SURRÉNALES,

Par le Dr E. BROWN-SÉQUARD.

Lauréat de l'Académie des Sciences,
Vice-Président de la Société de Biologie, etc.

Extrait des Archives générales de Médecine,
numéro d'octobre 1856 et suivants.

PARIS.

RIGNOUX, IMPRIMEUR DE LA FACULTÉ DE MÉDECINE,
rue Monsieur-le-Prince, 31.

1856

FIG. 3. Title page from the publication of Brown-Séquard in which he describes the first adrenalectomies in animals.

palpation of the adrenals preparatory to excision. Hugh Young, in 1936, turned the patient to a prone position for a simultaneous bilateral approach. Very little new has been added to the technique since then. Slight modifications have been suggested: the posterolumbar route by Walters and Kepler, the posterolateral route by Huggins and his coworkers (9, 10), and the lateral subcostal route by Zintel and his associates, but the operation of adrenalectomy has continued to be moderately hard.

In more recent times, the influence of adrenocortical hormones on malignant lesions of the breast and prostate have become better understood, and, with adequate adrenocortical hormones for replacement therapy, total adrenal ablation in the human has become possible. Huggins and Scott (10), in 1945, reported the first total bilateral adrenalectomy for carcinoma of the prostate, and since then the operation has become commonplace. Our knowledge of adrenal anatomy is now complete. Much remains, however, to be learned of the function of these tiny bits of tissue. It has taken almost 500 years to bridge the gap between the discovery that the adrenal glands even existed and survival of humans after their complete excision. The vast unknown has yielded important and fascinating facts. It is hoped that in far less than a half century we will fathom the depths completely.

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Reviews of New Books

THE MONOGRAPH entitled *The Surgical Treatment of Scoliosis*[1] is one of the American lecture series in orthopedic surgery. In this volume of 100 pages, the author has based the material upon his experience during a 20 year period with 37 cases of idiopathic curve, 23 of paralytic curve, and 4 of congenital curve; 1 additional case is listed under miscellaneous curve.

When one speaks authoritatively on the subject of scoliosis, a comparison is immediately made with other controversial orthopedic problems, for example, fractures of the femoral neck. Here, experience with hundreds, or even thousands, of individual patients is necessary in order that conclusions may be drawn as to the best or, at least, the most advisable method of handling the problem. John Cobb, has said so often, "per cent means per hundred." One must be careful not to draw conclusions when the total series in one's experience is small. The author follows very closely the philosophy and technique of Cobb in selection and cast correction of the curve, even to the point of duplication of the curved Goldthwaite bars devised by Cobb for attachment to the fracture table in the application of the large turnbuckle cast. Perhaps the text would have been improved if more credit had been given to Cobb than is offered.

It is of interest that of 4 patients with "thoracolumbar" curves, only 1 retained correction while in 2 complete loss of correction occurred. Orthopedic surgeons with vast experience in scoliosis recognize the fact that thoracolumbar curves offer the greatest challenge, both from a standpoint of incidence of pseudarthroses at the eleventh thoracic and second lumbar areas and also from a standpoint of error in selection of the proper fusion area, particularly when the fusion is attempted in the younger age group. On the other hand, thoracic curves from the fourth to the eleventh thoracic level and from the fifth to the twelfth thoracic level usually fuse without many pseudarthroses occurring, and the chance of error in selection of the fusion area is much less. This author's experience in idiopathic scoliosis bears this out, since most of the good results were with thoracic curves.

Past experience in correction and fusion in the young scoliotic patient has been disappointing to some orthopedic surgeons. The author has carefully avoided this pitfall by selecting for correction and fusion only patients 12 years of age or older. In his series of patients with idiopathic scoliosis, only 1 was under the age of 11 years and 6 months at the time of fusion. One patient (Fig. 23) obviously lost all, or nearly all, correction because of a short fusion and subsequent lengthening of the curve which was only partially fused. The author's advice is to retain the original vertebrae of the curve in the final measurement. This gives a marked statistical advantage with less recorded loss of correction than is actually clinically present. This same error has crept into other illustrative cases (Fig. 26). In some instances, the author blames "overcorrection" for loss of correction, whereas a short fusion or, perhaps, pseudarthroses not readily discernible might be the more logical explanation. Failure to fuse both curves in a double structural curve has also led to similar pitfalls.

Orthopedic surgeons experienced with scoliosis are becoming increasingly aware of the problem of the young patient with a progressive curve. In many paralytic curves and in some curves of other origin, the question of early correction and fusion assumes a role of major importance. This monograph does not touch upon this problem. Likewise, major problems of correction and fusion in the patient with collapsing trunk, who is also a poor surgical risk from a standpoint of pulmonary function, is not discussed.

All in all, this monograph represents one man's rather limited experience with a method of correction and fusion of the older age group of scoliotic patients with relatively uncomplicated curves. To orthopedic surgeons with vast experience and unbiased opinions of the relative values of various methods of correction, it offers a worthwhile document of an honest and sincere effort to help the deformed scoliotic. To those less experienced, it offers a carefully described method which is of value and which is an entirely acceptable method of treatment. To many orthopedic surgeons, the author's method would seem to be the hard way to handle scoliosis. —*John H. Moe.*

A BOOK which many have been familiar with for some time in its first edition is the *Atlas of Roentgenographic Positions* by Merrill. The second edition[2] is a good textbook for the student technician as well as a fine reference for those more experienced. One major criticism of the volume, however, is that it lacks emphasis upon radiation protection. The techniques in the use of cones is not discussed and none of the illustrations shows cones on the equipment being utilized. There is no discussion of gonadal shielding and little, if any, emphasis on high filtration and high kilovoltage techniques. —*Bernard J. O'Loughlin.*

IN THE MONOGRAPH *Sexual Impotence in the Male*[3] Wershub classifies the impotent male into 3 etiologic groups for purposes of therapy. These groups are as follows: (1) those impotent because of organic reasons; (2) those impotent because of organic and functional causes; and (3) those with purely functional impotence.

[1]THE SURGICAL TREATMENT OF SCOLIOSIS. By Louis A. Goldstein, M.D., F.A.C.S. Appendix, Anesthesia in Scoliosis. By D. Vernon Thomas, M.B., F.F.A.R.C.S. 116 pages, illustrated. $6.75. Springfield, Ill.: Charles C Thomas, 1959.

[2]ATLAS OF ROENTGENOGRAPHIC POSITIONS. By Vinita Merrill. Vol. I—1-292, Vol. II—293-664. 2nd ed. Illustrated. $32.50. St. Louis: The C. V. Mosby Co., 1959.

[3]SEXUAL IMPOTENCE IN THE MALE. By Leonard Paul Wershub, M.D., F.A.C.S., F.I.C.S. Foreword by Ralph E. Snyder, M.D. 126 pages, illustrated. $5.75. Springfield, Ill.: Charles C Thomas, 1959.

The chapter on organic causes is comprehensive and a delight to read. When the "quasi organic" and functionally impotent male are discussed the author is, by his own admission, on controversial ground; but advice on the "positive" approach to such individuals is probably well taken.

There were some minor defects in this otherwise meritorious publication. In several instances, authors were mentioned and indexed, but the actual references were not cited. The retention of the word phallos, the Greek spelling of phallus, is not accepted by Webster or the Oxford English dictionary. The discussions in Chapter 3 concerning sexual excitement, erection, intromission, and ejaculation seemed unnecessarily superficial for a tract professedly aimed at physicians. None the less, the book is worth while for anyone called on to advise males upon this complex problem. —*Julian S. Ansell.*

THE NEW EDITION of Adler's *Physiology of the Eye*[4] is most welcome because it had been a bible for graduate students of ophthalmology and because the second edition has been out of print for some time. The general format of earlier editions is followed, but all of the material has been brought up to date. The new edition constitutes an entire revision with considerable new material and many recent references. It reflects, too, the increase in research concerning the eye during the past decade.

When Adler first wrote *Clinical Physiology of the Eye* in 1930, it was possible to encompass the field in a relatively brief text. Now, however, there is not only considerable data available but much of it is conflicting, so that it is necessary for the author to be quite selective in respect to the material used. Adler has made this selection judiciously and fairly and presents the generally accepted concepts of most ocular physiologic functions. The book has not been written as an all inclusive reference but presents, rather, the author's viewpoint concerning physiologic functions and their clinical significance. Completely apart from its value as a textbook this volume constitutes interesting and valuable reading for the practicing ophthalmologist. The writing is literate, the diagrams explanatory, and the publisher has fulfilled his functions expertly. —*Frank W. Newell.*

THE SUBJECT of the volume entitled *Clinical Applications of Diagnostic and Therapeutic Nerve Blocks*[5] is presented in such a manner as to encourage even the busiest practitioner to become acquainted with it and, consequently, use it to the advantage of the patient. The aim of the book is to present an evaluation of various nerve block procedures as diagnostic and therapeutic tools. An attempt has been made to present an objective assessment of the indications, effectiveness, advantages, as well as the disadvantages, complications, and limitations of these techniques. The chapters in the first section are devoted to certain general considerations concerning the clinical applications of nerve blocks in the management of disease. This material forms the basis for a discussion of the use of specific nerve block techniques.

It should be stressed that the book is intended for use by any practitioner interested in this problem. Although the anesthesiologist, having acquired a certain dexterity in executing nerve blocks for surgical anesthesia, is most frequently requested to perform these procedures on medical patients, many of these methods can and should be learned and practiced by every clinician. —*John S. Lundy.*

IN THE VOLUME entitled *The Triumph of Surgery*,[6] Jürgen Thorwald has woven the major developments in surgery during the last two decades of the nineteenth century and the first decade of the twentieth century into an exciting and fascinating story through the use of an unusual device. This has been accomplished by a fictitious eyewitness, an American physician named Hartmann, whose aim is to chronicle at firsthand the revolutionary changes in the art and science of surgery as they unfold. The book reads like a novel; but it is well documented, and the reference sources are listed in an extensive bibliography. The personalities of such great names in surgery as Halsted, Bassini, Kocher, J. B. Murphy, Mikulicz, Sauerbruch, and others are so cleverly and vividly portrayed that one gets to know them as real men rather than as the semimythologic figures they sometimes seem to be. At times, one gets the idea that a few of the characters may have been painted somewhat larger than life-size in their conceit, in their inflexibility, and in their fearful wranglings over prestige, priority of ideas, the value of new developments, and the like. But this does not detract from the book; indeed, it makes the characters more memorable.

The scope of the book is fairly wide. It describes many of the advances in neurosurgery from the time that Farrier conclusively demonstrated the localization of functional centers in the brain. It presents the history of the development of thyroid surgery very dramatically. It tells the story of biliary tract surgery from Bobb's first cholecystostomy done in Indianapolis in 1867 to Langenbuch's first successful cholecystectomy performed in Berlin in 1882. It lists the events leading to the discovery of the local anesthetic agents and the development of local, conduction, and spinal anesthesia. It also deals with the beginning of thoracic surgery, describing how Sauerbruch eventually solved the problem of pulmonary ventilation in the patient with an open thorax by using a negative pressure cabinet which housed the patient, except for his head, as well as the whole surgical team; and it describes the eventual perfection of the much simpler system of positive pressure ventilation.

The Triumph of Surgery will be enjoyed by the surgeon and layman alike. Thus, while the basic principles and problems, as well as the technical features related to each advance in surgery are explained sufficiently to let one who is unfamiliar with the subject understand the significance of the contribu-

[4]PHYSIOLOGY OF THE EYE; CLINICAL APPLICATION. By Francis Heed Adler, M.A., M.D., F.A.C.S. 3rd ed. 790 pages, 372 illustrations. $16.00. St. Louis: The C. V. Mosby Co., 1959.

[5]CLINICAL APPLICATIONS OF DIAGNOSTIC AND THERAPEUTIC NERVE BLOCKS. By John J. Bonica, M.D. 354 pages, 45 illustrations. $8.75. Springfield, Ill.: Charles C Thomas, 1959.

[6]THE TRIUMPH OF SURGERY. By Jürgen Thorwald. Translated by Richard and Clara Winston. 454 pages, illustrated. $6.50. New York: Pantheon Books, Inc., 1960.

tion, this information is introduced into the narrative in such a way as to keep even the well informed surgeon's interest high.

Thorwald's first book on the history of surgery, *The Century of the Surgeon*, should be mentioned here. Written in the same style, in the first person of the same fictitious Dr. Hartmann, it too is a fascinating account of the men who had the leading roles in the advance of surgery in the last century. It deals primarily with the 2 most important developments in modern surgery: the discovery and application of general anesthesia to surgery, and the gradual introduction and grudging acceptance of the antiseptic technique and, eventually, of the principle of asepsis.

—*Edwin L. Brackney.*

THE SECOND EDITION of the book entitled *Radiologic Examination of the Small Intestine*[7] in its first edition, proved an outstanding reference source. In this second edition, the references are brought up-to-date and many new illustrations demonstrate the better visualization possible with the aid of nonflocculating preparations of barium sulfate.

One of the outstanding features of the book is the extensive discussion of the embryology, anatomy, physiology, and roentgenographic appearance of the normal small intestine. The autonomic nervous control of the intestine and the effects of drugs and food are described in detail. The importance of understanding the physiology of the small intestine for interpreting the many diverse patterns encountered upon roentgenographic examination is particularly stressed. All of the common diseases of the small intestine are extensively reviewed, as are many of the uncommon disorders, and the reproductions are of well selected roentgenograms. A chapter on the Miller-Abbott tube and the diagnosis and treatment of ileus, and another on the small intestine after surgery, should be of particular interest to surgeons.

The author reviews various techniques for performing roentgenographic examinations of the small intestine, and advocates the use of nonflocculating barium preparations and high kilovoltage with fluoroscopy, multiple films, and spot films, with and without pressure. The water soluble opaque materials are considered as unsatisfactory for examination of the small intestine.

This volume should be of great value to roentgenologists, gastroenterologists, surgeons, and general practitioners as an authoritative reference source in all diseases of the small intestine.

—*Howard L. Steinbach.*

THE BOUND VOLUME entitled *The American Academy of Orthopaedic Surgeons; Instructional Course Lectures*[8] has been published annually, initiated in 1943 by J. E. M. Thomson. The present volume deserves special mention because it is the first in this series to be printed by The C. V. Mosby Company, and there is a radical departure in format from previous volumes. This new volume is attractively printed and contains excellent illustrations. The quality of the paper and the binding are superior. The Editor, Fred C. Reynolds, has selected 26 lectures for publication which have been assembled in 7 chapters. The lectures are all highly specialized and directed to orthopedists. Although much of the material has already been presented in the literature, it is worth rereading. It is refreshing to see some new names among the list of lecturers, and, consequently, to find some new points of view on orthopedic problems. Reynolds and the publishers deserve the thanks and the patronage of orthopedists everywhere; the former for flexing his editorial muscles effectively; the latter, for the attractive packaging.

—*Leonard F. Peltier.*

THE POCKET-SIZED HANDBOOK, *Diseases of the Nose, Throat, and Ear*,[9] obviously designed for undergraduates and general practitioners has apparently been a popular one in England, if the fact that a seventh edition is a good criterion.

The book is characterized by: (1) the mention, at least, of most everything that pertains to modern otolaryngology; (2) a very limited treatment of most subjects; (3) more space devoted to an outline of the steps in surgical therapy than to the rationale for performing these operations; and (4) a relatively small number of illustrations.

—*Lawrence R. Boies.*

AS THE SUBTITLE IMPLIES, the monograph *Peripheral Facial Palsy; Pathology and Surgery*[10] deals thoroughly with the pathologic considerations in the etiologic sphere and the major emphasis is upon the surgical treatment of these lesions.

The author states: "The present study deals exclusively with cases of peripheral facial palsy in which surgical intervention may be needed or has been suggested and was technically practicable." Brief, but sufficient, descriptions of general considerations in the degeneration and regeneration of peripheral nerves are included. Relatively more thorough descriptions of the anatomy and physiology of the facial nerve, including the clinically important description of its blood supply at various levels, are given in the basic portions of the monograph.

The author, who is the chief surgeon of the Department of Otolaryngology at Frederiksborg Central Hospital in Hilleroid, Denmark, bases his work largely upon personal experience with 311 surgical patients suffering from peripheral facial palsy.

Almost half of these operations were for decompressions for Bell's palsy. Numerous other decompressions were performed for Melkersson's syndrome, hemifacial spasm, otitic facial palsy, fractures of the temporal bone, carcinoma of the middle ear, and various traumas.

[7] RADIOLOGIC EXAMINATION OF THE SMALL INTESTINE. By Ross Golden, M.D. 2nd ed. 560 pages, 176 illustrations. $28.50. Springfield, Ill.: Charles C Thomas, 1959.

[8] THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS; INSTRUCTIONAL COURSE LECTURES. Edited by Fred C. Reynolds, M.D. Vol. XVI. 335 pages, illustrated. $16.00. St. Louis: The C. V. Mosby Co., 1959.

[9] DISEASES OF THE NOSE, THROAT, AND EAR. A HANDBOOK FOR STUDENTS AND PRACTITIONERS. By L. Simson Hall, M.B., Ch.B., F.R.C.P.E., F.R.C.S.E. 7th ed. 467 pages, illustrated. $5.00. Edinburgh and London: E. & S. Livingstone Ltd., 1959; Baltimore: The Williams & Wilkins Co., exclusive U.S. agents.

[10] PERIPHERAL FACIAL PALSY; PATHOLOGY AND SURGERY. By Karsten Kettel, M.D. Foreword by Terence Cawthorne, F.R.C.S. 341 pages, illustrated. $19.50. Springfield, Ill.: Charles C Thomas, 1959.

Seventy-eight cases involved either nerve grafting or nerve suturing to correct paralyses after various forms of trauma, either surgical or otherwise.

The work is well organized and specific indications and technical methods for each of the pathologic entities considered are given by the author. Excellent illustrations, both in the form of diagrammatic drawings and even numerous colored photographs of the operative fields, increase the value of the work.

A brief discussion only of the intracranial lesions of the facial nerve, particularly those resultant from the surgical removal of acoustic neuromas, is given.

The book is not indexed, but an extremely detailed table of contents, to some extent, makes up for this lack. Thirty-four pages of references would seem to constitute an extremely complete bibliography of the subject matter which should be of value to researchers in this field.

The contents of the book should be of great interest to neurologists and neurosurgeons, as well as to the otolaryngologist and to the plastic surgeon.

—Hale Haven.

IN *A Textbook of Surgical Physiology*,[11] Jamieson and Kay have endeavored "to discuss only those aspects of applied physiology which are fundamental to the practice of general surgery." Their purpose was to fill the needs of the postgraduate student and, in this, they have succeeded rather well.

The 610 pages of the text are divided into 26 chapters: "Wound Healing," "Biologic Effects of Radiation," "Fluid Balance," "Metabolic Response to Trauma," "The Adrenal Gland," "The Breast," "The Thyroid," "The Respiratory System," "The Heart," "The Circulation," "The Blood," "The Spleen," "The Lymphatic System," "Peripheral Nerves," "Bone," "Vitamin B Complex," "Stomach," "Small Intestine," "Colon," "Liver," "Gallbladder and Bile Ducts," "Pancreas," "Kidney," "Ureter," "Bladder," and "Testis." In general, the 186 illustrations emphasize clearly the points at issue. The relatively few selected references at the end of each chapter are well chosen, and, for the most part, they represent the outstanding contributions in the particular field under consideration.

The volume is well balanced from the point of view of giving deserving emphasis to the various segments of surgical physiology. The style employed makes for easy reading, and a common sense approach to clinical surgery is clearly apparent throughout.

Whereas in the preface the authors make specific mention of their omission of chapters on the central nervous system, the ovary, and the pituitary, one could have little criticism on this point, since the nervous system is well represented in the different chapters in which it applies to the subject under discussion. There is no particular reason to discuss ovarian physiology in a textbook of surgical physiology for general surgeons, and the only omission of the three which might need to be added in a subsequent edition is that of the pituitary—inasmuch as it appears that surgeons will be more and more concerned with the endocrinologic modification of neoplasia.

As this reviewer is well aware, it is essential to have a definite cut-off date, with the hope that information which subsequently becomes available can be included in the next edition. Thus, reference to the following omissions is made largely to direct attention to them so that they can be corrected in later editions of this sound text. First, the statement that "no method of preparing fat for intravenous administration has yet been found" would, to say the least, bear qualification. Intravenous fat preparations have been widely used in the United States, at least on an experimental basis, and it would perhaps be more accurate to say that preparations suitable for routine clinical therapy are not yet available. Second, in another section it is stated that it has not been possible to demonstrate the presence of androgens and estrogens in adrenal vein blood. While the evidence for the presence of these hormones is thus far largely chemical in nature, it is probably safe to say that the presence of these hormones has been established; in fact, such data have been recorded in the literature. Third, the section on lung function might be made somewhat more specific.

All in all, this reviewer is happy to endorse the volume. It includes a considerable amount of material which most practicing surgeons would probably have known as normal physiology, and this may have, at times, displaced more advanced information dealing with disease states. However, everything cannot be offered to everyone in a single volume, and one believes that the authors have accomplished what they set out to do.

—James D. Hardy.

TO REVIEW an encyclopedic work in a few paragraphs is admittedly an impossible task, and to give an adequate picture of Gordon's *Medieval and Renaissance Medicine*[12] in a limited space is almost as difficult. Names, places, and dates fly by in rapid succession and unless one reads slowly, and often a second time, the reader may be left with a very hazy and blurred mental picture.

The author's material is presented first in chronologic order, and the first 10 chapters take the reader from the fall of Rome to the close of the Arabo-Spanish Period, approximately 1200 A.D. The chapters on Arabian medicine are especially well written, and Rhazes, Avicenna, Albukasim, Averroes, and Maimonides stand out as distinctive individuals.

Chapters on "Jewish Contributions to Medicine in the Middle Ages," "Scholasticism and Medicine," an interesting account of the "Invention of Spectacles" and a chapter on the "Rise of the Universities" are followed by 5 chapters on "Medieval Medicine in Italy, France, England, Germany, and Russia," a chapter on "Anatomy," another on "Surgery," and then a series of chapters on specific diseases—epidemic diseases, tuberculosis, and smallpox. In the final chapters, 33 to 44, the author traces the gradual change that culminated in what is termed the Renaissance.

[11] A TEXTBOOK OF SURGICAL PHYSIOLOGY. By R. Ainslie Jamieson, M.B., F.R.C.S. Ed., and Andrew W. Kay, M.D., Ch.M., F.R.C.S. Ed., F.R.F.P.S.G. 623 pages, 186 illustrations. $11.00. Edinburgh and London: E. & S. Livingstone Ltd., 1959; Baltimore: The Williams & Wilkins Co., exclusive U. S. agents.

[12] MEDIEVAL AND RENAISSANCE MEDICINE. By Benjamin Lee Gordon, M.D., F.I.C.S. 843 pages, illustrated. $10.00. New York: Philosophical Library, Inc., 1959.

The change from a chronologic order to a discussion of varied subjects, diseases of national characteristics, and of medical specialties leads to considerable repetition, and to a certain lack of clear delineation of the individuals who are the main actors in the scene. For example, in the index there are 12 references to William Harvey, but nowhere does one get a clear concept of the man and how he arrived at the conclusions which lead to his *de Motu Cordis*.

There are some surprising omissions. No mention is made of Taliacotius, or his forerunners, the Brancas, although Gnudi and Webster made the Italian surgeon the subject of a 500 page volume devoted to his life and times.

The outstanding impression that Gordon's history leaves with the reader is of the cruelty, ignorance, viciousness, and immorality of man during the medieval era. One wonders as to the authority for some of his statements; for example (p. 14), "Even the Vestal Virgins were guilty of inconceivable immoralities," and (p. 431), with reference to the practice of emasculation, "It is estimated that 35,000 children were annually sacrificed to produce the Sudanese average quota of 3800 eunuchs per annum."

Surely there were many, many individuals and many physicians in those admittedly Dark Ages who heard and heeded the words of the Man who said, "Blessed are the pure in heart." If in 2960 a historian judged our era by the reports on the first page of many of our newspapers he perhaps would find little to commend, but we would not agree that it would be a true picture of our life and times.

—*Sumner L. Koch.*

DETAILED INFORMATION on the technical aspects of producing x-ray motion pictures is presented in the volume, *Cinefluorography*.[13] The book is a transcription of the proceedings of the First Annual Symposium on Cinefluorography at Rochester, New York in November 1958. Included are data on the currently available forms of image intensifiers, recording equipment, and projection equipment. A section is devoted to television circuitry. Discussions of experimental techniques, such as electro-optical image intensification, solid-state amplifying screens, and fiber-optics are also presented.

There is some overlapping of material as may be expected in a volume of multiple authorship. A few of the papers are less than entirely lucid. However, the volume represents a unique opportunity to review the technical aspects of this exciting development in roentgen diagnostic techniques. Furthermore, practical information concerning the use of image intensifier equipment and the choice of lenses, cameras, films, developing materials, and projectors makes this a most worthwhile source of information for those individuals who are interested in this subject.

—*Richard G. Lester.*

[13]CINEFLUOROGRAPHY. Proceedings of the First Annual Symposium on Cinefluorography, Sponsored by the Department of Radiology, University of Rochester, School of Medicine and Dentistry, Rochester, New York, Friday and Saturday, November 14 and 15, 1959. Edited by George H. S. Ramsey, M.D., Theodore A. Tristan, M.D., James S. Watson, Jr., M.D., Sydney Weinberg, and William S. Cornwell, M.A. 266 pages, illustrated. Springfield, Ill.: Charles C Thomas, 1959.

EVERY SURGEON will be interested in the well written book entitled *Surgery as a Human Experience*[14] which is aimed at broadening his insight into the patient's experience as it pertains to the illness leading to surgical intervention on through to the total outcome of the doctor-patient relationship. Written from a multidimensional viewpoint, *Surgery as a Human Experience* presents an elementary foundation for the understanding of the behavior of a broad range of patients selected at random from the wards of the Cincinnati General Hospital. Since the technical aspects of the surgery is not referred to, nor is a special issue made regarding the severity or area involved, except in Chapter 9, the main focus is on the behavior aspects of any patient in the surgical situation. Thus, it strikes me as a general orientation text with an excellent selective review of the current literature without cumbersome detail and devoid of speculative issues. It could easily be the pilot book of a series that would examine more specific types of surgery.

The development of dynamic psychology is reviewed and applied for the reader so that a native intuition can be sharpened into a penetrating empathic grasp of the situation in which surgeon and patient live during their therapeutic alliance. The psychologic physiologic and sociologic balances are examined drawing freely upon experiences of other workers as well as the Cincinnati team. If the reader is interested he may explore the carefully selected bibliography. Of the very important issues considered, the following are discussed in understandable terms: (1) Why do patients deny illness until it is too late? (2) Why do patients seek surgery for the fulfillment of neurotic needs? (3) What is the pain experience? (4) Why do some people get worse or develop new symptoms after successful surgery? (The negative therapeutic response.) (5) How does the psychosomatic idea apply to surgery?

Many hints on the management of psychologically poor adaptations to the surgical experience are reviewed which initiates some considerations of the surgeon's role during the total therapeutic relationship.

—*John C. Todd.*

THE MONOGRAPH of 198 pages dealing with the problem of male infertility is entitled *Praktische Spermatiologie ein Leitfaden fuer Aerzte*.[15] Although this volume is concerned mainly with the evaluation of the semen, the entire field of male infertility is discussed.

The author, in addition to an exhaustive and critical review of the literature, has obviously drawn upon a large experience and much personal research.

In spite of its brevity, this book is almost encyclopedic in scope. It is so well written that a tremendous amount of highly technical, morphologic, physiologic, biochemical, and endocrinologic material is presented in a pleasant, easily readable style. The information presented is accurate and up-to-date.

[14]SURGERY AS A HUMAN EXPERIENCE. THE PSYCHODYNAMICS OF SURGICAL PRACTICE. By James L. Titchener, M.D., and Maurice Levine, M.D. 285 pages. $6.00. New York: Oxford University Press, 1960.

[15]PRAKTISCHE SPERMATIOLOGIE EIN LEITFADEN FUER AERZTE. By Priv. Doz. Dr. Med. H. W. Vasterling. Foreword by Prof. Dr. Heinz Kirchhoff. 224 pages, 86 illustrations. $6.40. Stuttgart: Georg Thieme Verlag, 1960.

There are 85 superb illustrations; the bibliography includes 525 references.

This is, without question, one of the finest monographs on the subject that the reviewer has seen.

Although this volume is eminently practical, it should appeal especially to investigators in the field of study of the problem of male infertility.

—*Frederick A. Lloyd.*

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

Outline of Orthopaedics. By John Crawford Adams, M.D.(Lond.), F.R.C.S.(Eng.). 3rd ed. 440 pages, 313 illustrations. $8.00. Edinburgh and London: E. & S. Livingstone Ltd., 1960; Baltimore: The Williams & Wilkins Co., exclusive U. S. agents.

Surgery of Repair as Applied to Hand Injuries. By B. K. Rank, C.M.G., M.S.(Melb.), F.R.C.S.(Eng.), F.R.A.C.S., and A. R. Wakefield, M.S.(Melb.), F.R.C.S.(Eng.), F.R.A.C.S. Foreword by Sir Gordon Gordon-Taylor. 2nd ed. 284 pages, 219 illustrations. $9.00. Baltimore: The Williams & Wilkins Co., 1960.

Surgical Anatomy of the Bronchovascular Segments. By William E. Bloomer, M.D., Averill A. Liebow, M.D., and Milton R. Hales, M.D. With a foreword by Gustaf E. Lindskog, M.D. 273 pages, 208 illustrations. $16.50. Springfield, Ill.: Charles C Thomas, 1960.

La endometriosis. By Dr. Donato Gonzalez Marmol. 359 pages, 43 illustrations. Havana, 1959.

Treatment By Manipulation and Massage. By James Cyriax, M.D.(Cantab.), M.R.C.P.(Lond.). 6th ed. 375 pages, 127 illustrations. $7.50. New York: Paul B. Hoeber, Inc., 1959.

The Cell of Schwann. By Gilbert Causey, M.B., F.R.C.S. Foreword by Sir James Paterson Ross. 120 pages, 40 illustrations. $4.75. Edinburgh and London: E. & S. Livingstone Ltd., 1960; Baltimore: The Williams & Wilkins Co., exclusive U. S. agents.

Osteochondritis Dissecans, Loose Bodies in Joints, Etiology, Pathology, Treatment. By I. S. Smillie, O.B.E., Ch.M., F.R.C.S.(Ed.), F.R.F.P.S. 224 pages, illustrated. $12.50. Edinburgh and London: E. & S. Livingstone Ltd., 1960; Baltimore: The Williams and Wilkins Co., exclusive U. S. agents.

Nine Months' Reading; a Medical Guide for Pregnant Women. By Robert E. Hall, M.D. 1919 pages, 13 illustrations. $2.95. Garden City, New York: Doubleday & Co., Inc., 1960.

Pyelorenal Reflux and Its Clinical Significance. By Anton Pytel. 272 pages, 114 illustrations. Moscow: State Publisher of Medical Literature, 1959.

Crash Injuries. By Jacob Kulowski, M.D., F.A.C.S., F.I.C.S. 1080 pages, 531 illustrations. $32.50. Springfield, Ill.: Charles C Thomas, 1960.

Archivio "Putti" di chirurgia degli organi di movimento. By O. Scaglietti and L. Gui. Vol. XII. 494 pages, illustrated. Florence: Edizioni Scientifiche dell' "Istituto Ortopedico Toscano," 1959.

Gynaekologen deutscher Sprache; Biographie und Bibliographie. By Walter Stoeckel. 3rd ed. 630 pages. Stuttgart: Georg Thieme Verlag, 1960.

The Thyroid-Vitamin Approach to Cholesterol Atheromatosis and Chronic Disease; a Ten Year Study. By Murray Israel, M.D. 132 pages. New York: George Press, Inc., 1960.

Medical, Surgical, and Gynecological Complications of Pregnancy. Edited by Alan F. Guttmacher, M.D., and Joseph J. Rovinsky, M.D. 619 pages, 47 illustrations. $16.50. Baltimore: The Williams & Wilkins Co., 1960.

Die Krankheiten des Neugebornen und Fruehgeborenen. By S. von Berlin-Heimendahl. 540 pages, 77 illustrations. Approximately $18.00. Stuttgart: Ferdinand Enke, 1960.

Postmortem Homografts. James Barrett Brown, M.D., F.A.C.S., and Minot P. Fryer, M.D., F.A.C.S. 64 pages, 25 illustrations, $5.50. Springfield, Ill.: Charles C Thomas, 1960.

A Dictionary for Medical Secretaries. By Isabel Alice Stanton. 175 pages. $6.50. Springfield, Ill.: Charles C Thomas, 1960.

Peptic Ulceration. By Charles Wells and James Kyle. Foreword by Lester R. Dragstedt. 260 pages, 41 illustrations. $8.75. London: E. & S. Livingstone Ltd.; Baltimore: The Williams & Wilkins Co., 1960.

Surgery and Clinical Pathology in the Tropics. By Charles Bowesman, F.R.C.S.E., F.A.C.S., D.T.M., and H.Ed. 1068 pages, 321 illustrations. $22.50. London: E. & S. Livingstone Ltd.; Baltimore: The Williams & Wilkins Co., 1960.

Fundamentals of Clinical Hematology. By Byrd S. Leavell, M.D., and Oscar A. Thorup, Jr., M.D. 503 pages, 71 illustrations. $10.00 Philadelphia: W. B. Saunders Co., 1960.

Edema, Mechanisms and Management. Edited by John H. Moyer, M.D., and Morton Fuchs, M.D. 833 pages, illustrated. $15.00. Philadelphia: W. B. Saunders Co., 1960.

AMERICAN COLLEGE OF SURGEONS

OWEN H. WANGENSTEEN, Minneapolis, *President*

I. S. RAVDIN, Philadelphia, *President-Elect*

PRELIMINARY PLANS FOR THE 46th CLINICAL CONGRESS CIVIC AUDITORIUM, SAN FRANCISCO, CALIFORNIA 10 TO 14 OCTOBER, 1960

THE JUNE ISSUE of this journal outlined in brief the scope of this year's Clinical Congress program. In this, and subsequent issues, program details will be filled in.

In the well-known Ciné Clinics, selected surgeons will demonstrate work for which they are distinguished, and they will be present to discuss these operations. The Surgical Products Division of American Cyanamid Company, Danbury, Connecticut, sponsors the Ciné Clinics. These color films will be seen Monday through Thursday. The advance schedule, listing the operation and operating surgeon, follows. Participants who will discuss each film will be listed later.

Siamese Twins. J. ENGLEBERT DUNPHY, Portland.
Intestinal Atresia. CLIFFORD D. BENSON, Detroit.
Hernia. WILLIAM L. ESTES, JR., Bethlehem, Pennsylvania.
Thyroidectomy. DAVID HENRY POER, Atlanta.
Fluid Balance in Gastrointestinal Surgery. ROBERT M. ZOLLINGER, Columbus.
Head Injuries. JOSEPH P. EVANS, Chicago.
Chemotherapy of Cancer-Limb Perfusion. OSCAR CREECH, JR., New Orleans.
Appendicitis. S. W. MOORE, New York.
Strangulation Obstruction. HAROLD LAUFMAN, Chicago.
Mesenteric Thrombosis. RICHARD L. VARCO, Minneapolis.
Prevention of Adhesions. JOHN ARMES GIUS, Iowa City.
Aortic Stenosis. HENRY T. BAHNSON, Baltimore.
Radical Wertheim Operation. JOE V. MEIGS, Boston.
Ureteral Injury. CHARLES C. HIGGINS, Cleveland.
Acute Large Bowel Obstruction. FRASER N. GURD, Montreal.
Surgery of Cancer of Colon. RUPERT B. TURNBULL, JR., Cleveland.
Carcinoma of Rectum. JONATHAN E. RHOADS, Philadelphia.
Regional Enteritis. LEON GOLDMAN, San Francisco.
Endoscopic Surgery of Bronchoesophageal Diseases. PAUL H. HOLINGER, Chicago.
Sympathectomy for Arthritic Pain. BEN EISEMAN, Denver.
Pedicle Grafts. PAUL W. GREELEY, Chicago.
Physiological Basis for Treatment of Duodenal Ulcer. R. CAMERON HARRISON, Edmonton.
Gastric Ulcer. CARLETON MATHEWSON, JR., San Francisco.
Total Gastrectomy for Carcinoma. JOHN M. BEAL, New York.
Cholangiography. LEON GOLDMAN, San Francisco.
Common Duct Repair. JAMES A. KIRTLEY, JR., Nashville.

On Wednesday evening, the popular program of short films known as the Symposium on Spectacular Problems in Surgery will be presented. The advance schedule follows:

Kidney Stone and the Parathyroid. HOWARD H BRADSHAW, Winston-Salem.
Splenectomy (4,200 Gram Spleen). WILLIAM D. HOLDEN, Cleveland.
Rupture of Stomach in Newborn. WILLIAM J. GROVE, Chicago.
Cushing's Disease in Infancy. E. STANLEY CRAWFORD and GEORGE CLAYTON, Houston.
Pneumatosis Cystoides Intestinalis. EDWIN H. ELLISON, Milwaukee.
Cartilaginous Spur (Exostosis) of Cervical Vertebra. JAMES D. HARDY, Jackson, Mississippi.
Anomalies of the Umbilicus. ROWENA SPENCER, New Orleans.

Aberrant Pancreas Obstructing Duodenum. WILLIAM H. REMINE, Rochester.

Myxoma, Intra-atrial. EGBERT H. FELL, Chicago.

Twenty-Four Pound Ovarian Cyst in Adolescent. HUGH B. LYNN, Louisville.

Juvenile Polyps of the Colon. HAROLD A. ZINTEL, New York.

Ulcerogenic Tumor of the Pancreas. ROBERT M. ZOLLINGER, WILLIAM PACE, and DAN ELLIOTT, Columbus, Ohio.

Myocardial Dynamics After Ventriculotomy. DENTON A. COOLEY and JOHN L. OCHSNER, Houston.

Tumor of the Left Ventricle. WILLIAM P. LONGMIRE, JR., Los Angeles.

Plastics in Plastic Surgery. JAMES BARRETT BROWN, St. Louis.

Thrombectomy in Acute Ileofemoral Venous Thrombosis. J. ALEX HALLER, JR., Louisville.

Parasitic Twin. COLIN C. FERGUSON, Winnipeg.

General Sessions

General sessions will begin Monday at 10 a.m. with Clarence J. Berne moderating a panel on "Acute Perforations of the Alimentary Tract," and, as panelists, Allen M. Boyden, James D. Hardy, and C. Barber Mueller.

From 1:30 to 3:30 p.m. "Tumors of the Pancreas" will be considered, with Robert J. Coffey as moderator and Richard B. Cattell, Walter C. MacKenzie, and Robert M. Zollinger as panelists. "Surgical Treatment of Obstructive Lesions of the Esophagus" will follow with Frederick G. Kergin moderating and John M. Dorsey, Donald B. Effler, and K. Alvin Merendino as panelists.

"Surgical Management of Cerebral and Visceral Arterial Occlusion" is the topic on Tuesday at 1:30 p.m., with Michael E. DeBakey as moderator, and Jack A. Cannon, E. S. Gurdjian, Robert S. Shaw, and Edwin J. Wylie as panelists.

The Symposium on Trauma will follow. Harrison L. McLaughlin, Chairman of the Committee on Trauma, will preside over the discussion on "Adjuncts to the Treatment of Trauma." Topics and speakers follow:

Use of Vessel Grafts and Prostheses in the Repair of Vascular Injuries. CHARLES A. HUFNAGEL.

Arteriography and Hypothermia in the Management of Head Injuries. FRANK H. MAYFIELD.

Use of Millipore in the Treatment of Peripheral Nerve Injuries. JAMES B. CAMPBELL.

Plastic Polymers in the Treatment of Fractures. CHARLES G. JOHNSTON.

A panel on "Management of the Patient with Carcinoma of the Breast" follows, with Ambrose H. Storck as moderator and Edward F. Lewison, Gilbert H. Fletcher, Bronson S. Ray, and Ian MacDonald as panelists.

On Wednesday at 1:30 p.m. Henry Swan will moderate a panel on "Recent Advances in General and Regional Hypothermia," with Ivan W. Brown, Ward O. Griffen, F. John Lewis, and James C. White as participants.

The Baxter Lecture will follow, with Leslie Philip Le Quesne of London, England, speaking on "Body Fluid Disturbances Resulting from Pyloric Dysfunction." The Cancer Panel will be next with a discussion of "Palliative Chemotherapy for the Cancer Patient," with R. Lee Clark, Jr., as moderator and Oscar Creech, Jr., George E. Moore, Anthony R. Curreri, and John Paul North as participants. A panel on "Acute Trauma of the Face and Head" will follow, with Jesse W. Mahoney as moderator and, as discussers, Bradford Cannon, James Barrett Brown, and John Raaf.

On Thursday at 1:30 p.m. "Prevention and Control of Infection in Abdominal Surgery" will be the topic, with Walter G. Maddock serving as moderator and W. A. Altemeier, J. Englebert Dunphy, J. F. Nuboer, and Edwin J. Pulaski as participants. The Graduate Training Symposium will be next, followed by the Trauma Oration, to be given by Joseph Trueta, Oxford, England, on "Trauma and the Living Cell."

What's New in Surgery will be held Friday at 9 a.m., with Harris B Shumacker, Jr., presiding. Speakers follow:

Neurological Surgery. BARNES WOODHALL.

Gastrointestinal Biliary Conditions. WILLIAM P. LONGMIRE, JR.

Plastic Surgery. JOSEPH E. MURRAY.

Tumors. HENRY T. RANDALL.

Anesthesia and Pulmonary Problems. JOHN H. GIBBON, JR.

Cardiovascular Surgery. H. WILLIAM SCOTT.

Urology. HUGH J. JEWETT.

Nutrition and Body Fluids; Shock and Burns. HENRY N. HARKINS.

Obstetrics and Gynecology. MILTON LAWRENCE MCCALL.

Specialty Panel Discussions

The preliminary program for these sessions follows:

GYNECOLOGY AND OBSTETRICS

MONDAY—Current Therapy of Toxemias of Pregnancy. T. N. EVANS, Moderator. Panelists: GORDON WATKINS DOUGLAS, CHARLES A. HUNTER, JR., and

ERNEST W. PAGE. Carcinoma of the Endometrium. S. B. GUSBERG, Moderator. Panelists: CHARLES E. MCLENNAN, JOE V. MEIGS, and JAMES F. NOLAN.

TUESDAY—Changing Aspects of Therapeutic Abortion. KEITH P. RUSSELL, Moderator. Panelists: RALPH J. GAMPELL, C. PAUL HODGKINSON, FRANK R. LOCK, and WESLEY T. POMMERENKE. Control of Conception. CHARLES S. STEVENSON, Moderator. Panelists: CELSO-RAMÓN GARCÍA, EDWARD T. TYLER, and ROBERT B. WILSON.

THURSDAY—Hydatid Mole and Choriocarcinoma. JOHN I. BREWER, Moderator. Panelists: PHILIP H. ARNOT, LEON P. FOX, and FREDERICK J. HOFMEISTER.

FRIDAY—Symposium. HARRY M. NELSON, Moderator. Endocrine Control of Uterine Contractility. ROBERTO CALDEYRO-BARCIA. Causes and Management of Prolonged Labor. RALPH A. REIS. Ten-Year End Results, Surgical Treatment of Carcinoma of the Cervix. LANGDON PARSONS. Ten-Year End Results, Radiological Treatment of Carcinoma of the Cervix. HANS-LUDVIG KOTTMEIER. Two panels follow: Shock and Shock-Like Reactions. EMIL J. KRAHULIK, Moderator. Panelists: MILTON J. MARMER, HOWARD E. SNYDER, DAVID STATE, and JOHN R. UPTON. Vaginal Approach to Pelvic Surgery. EUGENE A. EDWARDS, Moderator. Panelists: WILLIAM C. BRADBURY, HARRY BOYSEN, JOHN B. MONTGOMERY, and MILTON MCCALL.

UROLOGY

MONDAY—Concepts in the Management of the Neurogenic Bladder. HARRY M. SPENCE, Moderator. Panelists: ERNEST BORS, MYRON H. NOURSE, and DONALD R. SMITH.

TUESDAY—Fundamental Principles Underlying the Recognition, Prevention, and Management of Urinary Tract Infections. DONALD A. CHARNOCK, Moderator. Panelists: GRAYSON CARROLL, EDWARD N. COOK, and W. E. KITTREDGE.

WEDNESDAY—Management of Hydronephrosis. FRANK HINMAN, JR., Moderator. Panelists: WILLARD E. GOODWIN, FRANK C. HAMM, and PETER L. SCARDINO.

FRIDAY—Etiologic and Pathologic Mechanisms Underlying Neoplasia of Transitional Epithelium. WYLAND F. LEADBETTER, Moderator. Panelists: JAMES H. DEWEERD, F. K. MOSTOFI, and JAMES M. PRICE.

PLASTIC SURGERY

MONDAY—Principles in the Care of Traffic Injuries. PAUL W. GREELEY, Moderator. Panelists: FRANK F. KANTHAK, ALLYN J. MCDOWELL, and WILLIAM L. WHITE. Principles in Care of Cancer Patients. ROBERT M. MCCORMACK, Moderator. Panelists: FRANKLIN L. ASHLEY, CARL E. CHISM, CLAUDE C. COLEMAN, JR., and MILTON THOMAS EDGERTON, JR.

NEUROLOGIC SURGERY

FRIDAY—Shunt Procedures for the Relief of Internal Hydrocephalus. DONALD D. MATSON, Moderator. Panelists: IRA J. JACKSON, FRANK E. NULSEN, GEORGE PERRET, and ROBERT H. PUDENZ. Fluids, Electrolytes, and Steroids in Neurologic Surgery. JOHN R. GREEN, Moderator. Panelists: ROBERT L. MCLAURIN, W. EUGENE STERN, and BURTON L. WISE. Symposium, WILLIAM F. MEACHAM, Presiding. Intracranial Repair of the Injured Facial Nerve. CHARLES G. DRAKE. Discussion opened by FRANK J. OTENASEK. Intracranial Crushing of the Facial Nerve for Hemifacial Spasm. FLOYD H. BRAGDON. Plastic Encapsulation of Intracranial Aneurysms. BERTRAM SELVERSTONE. Discussion opened by EDGAR S. LOTSPEICH, JR. Vascular Anomalies of the Spinal Cord; Myelographic Aspects. HILLIER L. BAKER, JR. Surgical Aspects. HENDRIK J. SVIEN. Discussion opened by ROBERT C. BASSETT. Cerebral Vascular Insufficiency. HOMER D. KIRGIS. Discussion opened by RICHARD C. SCHNEIDER.

ORTHOPEDIC SURGERY

FRIDAY—Trauma of the Hand. LOT D. HOWARD, JR., Moderator. Panelists: JOSEPH H. BOYES, ROBERT E. CARROLL, and MORRIS J. DIRSTINE. Treatment of Femoral Neck Fractures and Complications. MARCUS STEWART, Moderator. Panelists: OTTO E. AUFRANC, CLINTON L. COMPERE, and ORVILLE N. JONES.

THORACIC SURGERY

FRIDAY—Recent Developments in Cardiovascular Surgery. F. HENRY ELLIS, JR., Moderator. Panelists: THOMAS G. BAFFES, HERBERT SLOAN, and FRANK COLE SPENCER. Tumors of the Lungs. DONALD L. PAULSON, Moderator. Panelists: PAUL C. ADKINS, J. MAXWELL CHAMBERLAIN, and ARTHUR M. OLSEN.

Fellows' Annual Meeting

The Annual Meeting of Fellows of the College will be held on Thursday, 13 October, at 3:45 p.m. In addition to the election of officers and Governors, there will be announcements and reports from officials. All Fellows are urged to attend.

Graduate Training Symposium

THURSDAY, 1:30–3 p.m., ROBERT M. ZOLLINGER, Columbus, Chairman.

Resident's Report Form. ROBERT M. MOORE, Galveston.

Basic Surgical Training. FRANK GLENN, New York.

Meeting Costs of Graduate Training. J. HARTWELL HARRISON, Boston.

Special Travel Arrangements

Convention representatives of the airlines and railroads participated in a meeting at the College headquarters to acquaint themselves with the scope of this Congress, and at which time they were requested to set aside a segment of their space for use of Fellows and guests traveling to San Francisco. As a result of this meeting, highly favorable travel arrangements have been obtained, and are outlined in the Invitation Brochure already mailed to Fellows and to non-Fellows upon request.

Advance Registration

Clinical Congress forms for advance registration, hotel accommodations, Postgraduate Courses, and transportation have been included in the Invitation Brochure mentioned. Early return of these forms is advisable to assure prompt receipt of your badge upon arrival, early choice of Postgraduate Courses, and satisfactory hotel or motel accommodations.

Fees

Fellows whose dues are paid to 31 December 1959 pay no registration fee; those whose dues are not paid as of above date pay $40.00. Non-Fellows will pay $40.00 if registered Sunday, Monday, or Tuesday; $30.00 if registered Wednesday; $20.00 if registered Thursday; $10.00 if registered Friday. Members of the Federal services will pay half of the above schedule of fees. No fee, except for Postgraduate Courses, is required of Initiates, members of the Candidate Group, and surgical residents. Everyone attending a Postgraduate Course pays a fee of $5.00. It is particularly requested that everyone wishing to attend carry identification—Fellowship, Candidate, Initiate—cards to the registration desk to expedite the registration process. Registration is limited to medical doctors and nurses.

Registration Hours

Registration hours at the Civic Auditorium will be:

SUNDAY, 9 October, 3 p.m. to 6:30 p.m.
MONDAY, 10 October, 8 a.m. to 5:30 p.m.
TUESDAY, 11 October, 8:15 a.m. to 5 p.m.
WEDNESDAY, 12 October, 8:15 a.m. to 5 p.m.
THURSDAY, 13 October, 8:30 a.m. to 5 p.m.
FRIDAY, 14 October, 8:30 a.m. to 5 p.m.

Ladies' Entertainment

Doctors are urged to bring their wives to San Francisco, for the Ladies' Entertainment Committee is planning an exceptionally interesting week. Among the events are included: Open House in six or seven of San Francisco's finest private homes; tours to Marin County, Muir Woods—the "giant Redwoods," University of California campus, Stanford University, Monterey, Carmel-by-the-Sea; Fashion Show; some selection of tickets for theatrical events in this city, including the San Francisco Opera and Ballet. An innovation this year: a "get-acquainted" tea on the opening day, Monday afternoon, as guests of the College.